Rs.10

JIMA

Volume 65 (RNI) ◆ Number 10 ◆ OCTOBER 2021 ◆ KOLKATA

JOURNAL *Of the* INDIAN MEDICAL ASSOCIATION

Official Publication of the Indian Medical Association

Indexed in

INDEX COPERNICUS INTERNATIONAL

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Volume 119 (JIMA) ♦ Number 10 ♦ October 2021 ♦ KOLKATA

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ISSN 0019-5847

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[2]Handin RI — Bleeding and thrombosis. In: Wilson JD, Braunwald E, Isselbacher KJ, Petersdorf RG, Martin JB, Fauci AS, *et al* editors—Harrison's Principles of Internal Medicine. Vol 1. 12th ed. New York: Mc Graw Hill Inc, 1991: 348-53.

Reference from Electronic Media :

[3]National Statistics Online—Trends in suicide by method in England and Wales, 1979-2001. www.statistics.gov.uk/downloads/ theme_health/ HSQ 20.pdf (accessed Jan 24, 2005): 7-18.

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JOURNAL
Of the
INDIAN MEDICAL ASSOCIATION

Volume 119 (JIMA)
Number 10
October 2021
KOLKATA
ISSN 0019-5847

Contents

(Continued next page)

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Contents

(Continued next page)

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Contents

Prof. Tamonas Chaudhuri
Hony. Editor
MBBS, MS, FAIS, FMAS, FACS, FACRSI (Hony)

Editorial

Research in.....

"To be, or not to be : that is the question :
Whether 'tis nobler in the mind to suffer
The slings and arrows of outrageous fortune
Or to take arms against a sea of troubles,
And by opposing end them ?"

This famous soliloquy spoken by Hamlet penned by the immortal author Shakespeare zeroes in on man's constant struggle for survival. Fighting against the volatile and hostile environment in which he lives the super ape is in incessant quest to find ways to ward off the predictable and mostly the unpredictable threats that conspires to annihilate him. The colossal dinosaur permanently retreated into the permanent extinction but not man, why? This is because they have learnt to adapt to the evolving time for which constant research and development is necessary. Dear all, needless to say the recent pandemic (COVID19) has shaken our confidence of survival from the very root and jerked us to the awareness that yet enough has not been done and lots remain to be achieved explored and implemented if man wishes to trod on this earth for many centuries to come.

Speaking from our Indian perspective we prefer to be blissfully ignorant about the onslaught of time and the hecatomb that has followed. The satanic cloud is still looming large yet the steps to combat it, adopted by us , is as trivial as David trying to defeat Goliath with his crude weapons. "BUT WHAT EXACTLY DO WE REQUIRE TO DO ?" your voice might blare out at me. I would shout back to you with equal gumption, 'RESEARCH AND DEVELOPMENT". Living in a fool's paradise is a luxury we cannot afford in the present time .

But what is Research and Development? The version used by Organisation for Economic Co-operation and Development (OECD)/Eurostat/UNESCO is as follows: Research and experimental development comprise creative work undertaken on a systematic base in order to increase the stock of knowledge, including knowledge about man, culture and society, and the use of this knowledge to devise new applications. The Frascati Manual is a document stating the

methodology for collecting statistics about research and development. Frascati Manual classifies research into three categories:

- Primary research is experimental or theoretical work undertaken primarily to gain new knowledge about observable phenomena and facts, not directed toward any specific application.
- Applied research is original investigation to acquire new knowledge directed primarily towards a specific practical aim or goal.
- Experimental development is systematic effort, based on existing knowledge from research or practical experience, directed toward creating novel or improved materials, products, devices, processes, system or services.

One of the greatest global health problems is that there is incoherence between the health research and development (R&D) that is required and that which is attempted. The dependence of health R&D on private sector and the lack of coordination between public and philanthropic funders on global R&D priorities have resulted in a global health R&D that is not 'needs-driven'. First demonstrated in 1990 it was shown that less than 10% of global health research expenditure was spent on the health problems of developing countries, which then represented more than 90% of the world's burden of preventable mortality (Fig 1)[1].

This neglect can be seen in the lack of R&D for diseases that predominantly affect developing countries (the 'neglected diseases'), in the lack of R&D that addresses the specific needs of developing countries in relation to diseases with a global incidence, and in the lack of development of affordable medicines for all[1]. But the problem of neglect extends beyond the developing world, as becomes clear from the global lack of R&D for new antibiotics, appropriate children's medicines (and other products), and orphan diseases. In addition to neglected populations, there are neglected products. R&D is generally more focused on the development of drugs and vaccines than on the development of diagnostics or platform technologies (technologies that can potentially be applied to different diseases and products). Moreover, for specific diseases, some products are neglected in terms of R&D, whereas others are not.

The trusted stop over for persons looking for data on health R&D is often the Government Budget Appropriations and Outlays for R&D (GBAORD) tables published by OECD and Eurostat. The Finance Minister, Government of India allocated Rs 2,663 crore to the Department of Health Research for the upcoming fiscal year 2021-22 in the Union Budget 2021. This is shockingly 34.4 per cent lower than Rs 4,062 crore, the revised estimate of health research expenditure

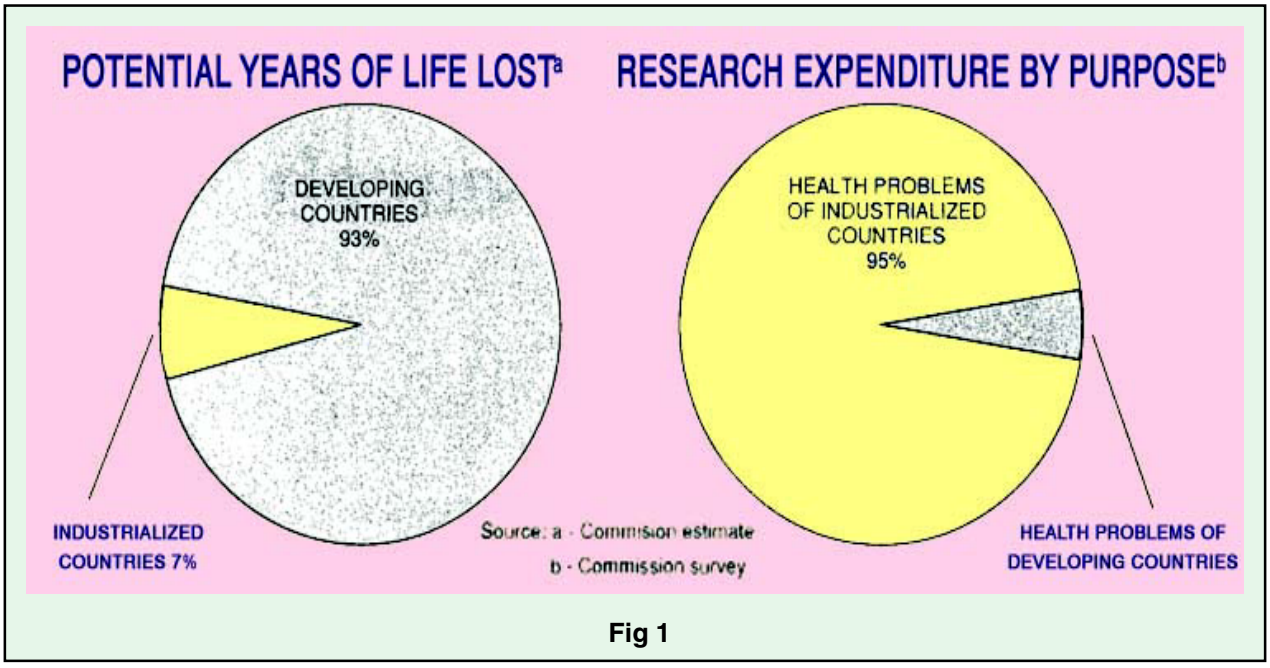

Fig 1

for 2020-2021[2]. Right at this moment when the coronavirus pandemic has forced world economies to spend considerably more on the research of emerging diseases and control, the government of India has significantly curtailed its budget allocation to health research. India expended 0.7 per cent of its Gross Domestic Product (GDP) on research and development in FY 18, while the same among other developing BRICS countries was - 1.3 per cent in Brazil, 1.1 per cent in Russian Federation, 2.1 per cent in China, and 0.8 per cent in South Africa[3].

These figures reflect that India is still behind other nations in terms of R&D. The total number of research and development projects in India in FY 19 was 11,640, which reduced to 11,170 in FY 20 and further nosedived to a meagre 3,491 in FY 21 so far, according to the Department of Science and Technology of India.

Although I have stated oodles of data to establish that a lot needs to be done to ensure proper research and development in health sector yet the role of INDIAN COUNCIL OF MEDICAL RESEARCH (ICMR) cannot be denied. The Indian Council of Medical Research (ICMR), New Delhi, the apex body in India for the formulation, coordination and promotion of biomedical research, is one of the oldest medical research bodies in the world. ICMR has made outstanding contribution as a knowledge generating agency and contributed in understanding various diseases of national importance such as malaria, Japanese encephalitis, tuberculosis, AIDS, Kala-azar, Filariasis, Leprosy and Poliomyelitis, Additionally, ICMR has made extensive contributions in the areas of nutrition, reproduction and maternal and child health, occupational and environmental health and research complimenting health systems. ICMR regional medical research institutes/ centres have been contributing in tackling regional health problems. ICMR is supposed to play a decisive role in tackling and annihilating the pandemic in India. Our indigenously developed vaccine "Covaxin" has been developed indigenously by Bharat Biotech International Ltd in collaboration with Indian Council of Medical Research (ICMR). ICMR is also helping Serum Institute of India [SII] in clinical trials as second sponsor agency.

With the repeated wave of nemesis we are left with no other option but to revamp and accelerate our research and developments so that we can nip the devil from its buds and establish a serene and tranquil environment for all the denizens of this earth. This is however only possibly if the governments of various countries respond to the urgency and mobilize enough funds for such research and developments to go on. There is no time for complacency. As dedicated warriors we have promises to keep

"And miles to go before I sleep,
And miles to go before I sleep."

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Original Article

Impact of COVID-19 Pandemic on Health Science Educational Institutions in Kerala

V V Unnikrishnan[1], Shalu Varghese[2]

The impact of COVID-19 has shaken the world to its core. Severe short-term disruption is felt by all domains of human existence. Educational institutions around the world are not spared. The national lockdown of health science education institutions caused major interruption in students' learning, both theory and practice; disruptions in internal assessments and the postponement of qualifying University examinations. In order to assess the magnitude and the extent of the impact of the catastrophe on the Health Science education sector in the state, the Kerala University of Health Sciences (KUHS), Thrissur, conducted online surveys among faculty members, students, educational experts and institution managers of affiliated institutions during April-May, 2020. The findings were analyzed to explore the possibilities; by integrating classroom learning with e-Learning modes to build a Unified Learning System, effective educational practice for the capacity building of young minds and some careful planning, we might be able to limit the long-term consequences of this prolonged shutdown.

[*J Indian Med Assoc* 2021; **119(10):** 17-21]

Key words **: COVID-19, Pandemic, Impact on Health Science Education, Online Teaching Learning, e-Learning.**

The COVID-19 lockdown has created unprecedented havoc in all the areas of human life globally. Academics is one of the key areas affected; disruptions have occurred in Theory and Clinical Training, Internal Assessments and Conduct of University Examinations.

The COVID-19 pandemic is primarily a health crisis. But its containment involves social measures which are all-encompassing. Like the rest of the World, India too decided to close down all schools, colleges and Universities along with industrial and commercial establishments- steps to reduce interpersonal contact[1]. Special Rules and Guidelines have been formulated for disease containment and 'Flattening of the Curve'. Situations and spaces for people aggregation have been limited. Public places like shops, malls, cinema and auditoriam are closed. By halting public transport and mass transit, free movements of citizens have been curtailed. Personal measures like wearing face masks and hand sanitizing are made mandatory for all. Infection spread is prevented by Sequestrating Containment Zones. Consequent to these measures, severe short-term disruptions are felt by many educational institutions around the World. The resulting home schooling-like situation is a massive shock to the students' social life, learning and career[2].

Kerala University of Health Sciences, Thrissur, Kerala 680596

[1]MBBS, MD, Professor and Dean (Academic) and Corresponding Author

[2]M Sc (N), Research Assistant

Received on : 23/06/2020

Accepted on : 04/09/2021

Editor's Comment :

- COVID-19 pandemic has created an intermediate to long term disruption in all domains of human life and the Health Science Education sector is critically affected.
- To overcome this situation, we need face the challenges head-on with meticulous, well grounded planning, effective allocation of available infrastructure and resources and utilising every opportunity to bring in innovations.
- Present scenario emphasizes the need to integrating classroom learning with e-Learning modes to build a Unified Learning System.
- Teachers and students need to be trained to explore digital learning, preferably using learning platforms which are open source rather than branded.
- Establishing a comprehensive and effective educational practice for the capacity building of young minds will develop skills which will upscale their employability, productivity, health and wellbeing in the decades to come.

Desperate situations require desperate measures. The present situation necessitates the stakeholders to move into online teaching, a less tried and tested modality of Teaching-learning Method in an unprecedented scale[3,4]. Student assessments might need to go online, which might further the uncertainty for everyone involved. As of now, many assessments have simply been postponed. Most importantly, these interruptions will not just remain short-term issues but can also have long-term consequences for the affected cohorts and are likely to increase inequality. The digital divide might widen further[5,6]. Even in the face of a number of hurdles,KUHS is trying to ensure online education initiatives so that students can continue their learning during the lockdown period and keep up the momentum of educational activities.

Material and Method

The KUHS was established for ensuring proper and systematic instruction, teaching, training and research in Modern Medicine, Homoeopathy, Dental, Nursing, Pharmacy, Indian Systems of Medicine including Ayurveda, Siddha, Yoga, Naturopathy, Unani and Allied Health Sciences. It provides uniformity in the various academic programs in the State of Kerala due to its state-wide jurisdiction. So far 312 professional colleges have been affiliated to the University. There are 13911 faculty members and nearly100,000 students studying in these affiliated Institutions. In our study, responses were obtained through Semi structured questionnaires from faculty members (n=3162), educational experts (n=18), managers (n=121) and students (n=4044). Google forms were used to collect and analyze the responses online.

Results

Impact of Lockdown : View of Teachers

Among the Health Science Faculty, 3162 teachers of Kerala University of Health Sciences affiliated Institutions participated in the study (Fig 1). 88.2% teachers opinioned that lockdown affected examination, 74.6% said it affected the classes (Fig 2). Since the Health Science Stream is practical oriented, other major area affected was clinical posting / practical experience, 11.41% teachers expressed their concerns regarding the loss of clinical hours. Fear of unemployment is shadowing the teaching and non-teaching members of staff within the Self Financing Health Science Education Sector. On the other hand, 53% of health science faculty members participated in online survey opinioned to continue online class after lockdown and they said online teaching learning activities are effective (Table 1).

Impact of Lockdown : View of Students

4044 students from different streams took part in the Survey (Fig 1). Among them, 67% students were from Private sector, 22% aided Colleges and 11% from Government sector. Most of the students (82%) were concerned about the restarting of their classes (Fig 3). 60.5% felt that regularity in their schedules got affected, 38.4 % said they were missing out the one-to-one interactions with their teachers, peers and friends. As many as 31.6 per cent students missed their extra-curricular activities such as Physical Education, Sports, Art, Music, and Dance (Fig 3).

Conversely, among students surveyed 55.5% per cent respondents stated that their concentration is better Studying at Home. 76.5% said online teaching is effective in supplementing in your regular learning, 63% suggested it is effective in bridging the learning gap caused by lockdown and 34% of health science students participated in online survey opinioned to continue online class after lockdown (Table 1).

Impact of Lockdown : View of Managers

The management representatives expressed concerns over the unexpected lockdown. It has affected all the domains of the education sector, creating a standstill. The impact of lockdown in the health science education sector resulted in some students contemplating on discontinuation of the courses. Financial concerns are looming in the background, especially since there are no patients in the hospitals. The financial constraint due to the lagging in fee collection also is a major challenge before the management to meet the two ends. If the lockdown

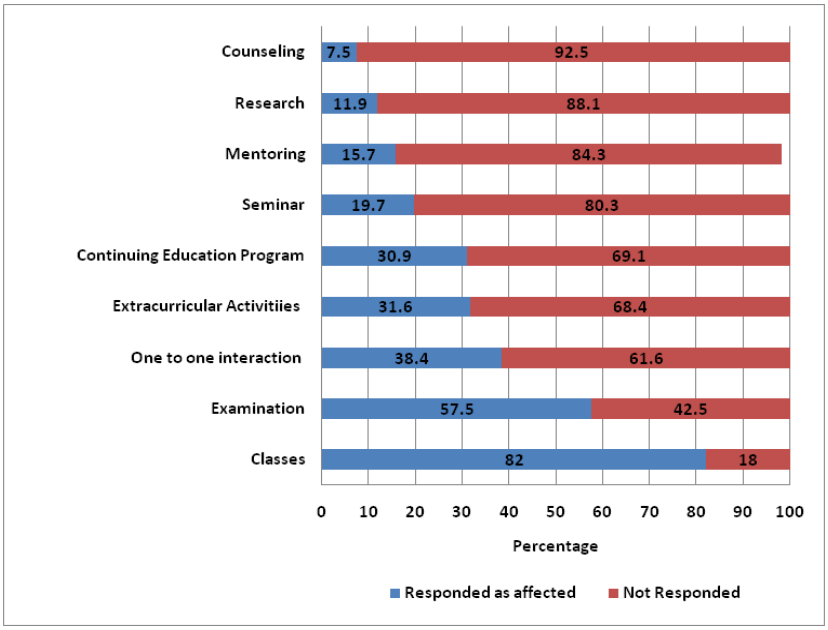

Fig 3 — Percentage Distribution of Health Science Students Participated in the Online Survey Based On Response Regarding the Academic Activities Affected by Lockdown
Fig 3 shows that most of the (82%) students participated in the survey responded as lockdown affected their classes, 57.5% responded examination got affected, 38.4% responded as lost one to one interaction with teachers, friends and at the least 7.5% said extracurricular activities became affected.

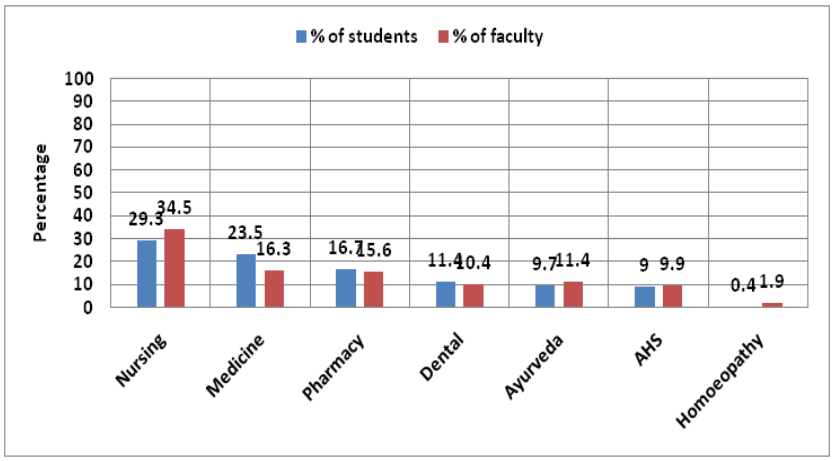

Fig 1 Percentage Distribution of Health Science Students and Faculty Members Participated in the Online Survey based on Stream

It is depicted in Figure: 1 that 29.3% of students participated in the online survey belongs to Nursing stream, 23.5 % from Medicine, 16.7 % from Pharmacy, 11.4% from Dental, 9.7 % from Ayurveda, 9% from Allied Health Science and 0.4 % from Homoeopathy stream,34.5% faculty members participated in the online survey belongs to Nursing stream, 16.3% from Medicine, 15.6% from Pharmacy, 11.4% from Ayurveda, 10.4% from Dental, 9.9% from Allied Health Science and 1.9% from Homoeopathy stream respectively.

goes on for the long run, management may find difficulty to pay the salary for the teaching and non-teaching staff.

Impact of Lockdown : View of Educational Experts

Lockdown affects all Govt, Aided and Self-financing Health Science Education Sectors. Lockdown has been implemented without prior notice because of that unable to plan the day-to-day activities of colleges. Health Science Education sector has virtually come to a grinding halt. Those functioning are with skeletal staff and virtually no students. Lockdown affected the academic activities, timely completion of the portions and the teaching- learning process to certain extent. The clinical exposure to students is non- existent. Quality of education is reduced. As far as the students are concerned, online classes are on and difficulties are alleviated to some extent. But in the case of managements, income generation is likely to be affected and they find difficulty to meet the expenses. In future it may affect the admissions and thriving prospects of colleges. In order to completely shift to a remote or online system, it is paramount to ensure that all students have or will be provided with the supportive infrastructure or resources, the findings noted.

Discussion

It is obvious that the Lockdown has comprehensively affected the Health Science Education Sector. This is clear from the views and concerns of all stakeholders. The affected include Academic, Financial and Social Sectors.

(1) Academic : The most important aspect is naturally, the Teaching, Learning and Examinations. The absence of public transport, conversion of hostels into quarantines, closing down of class rooms have resulted in stoppage of conventional systems. Students are justified in expressing their anguish over absence of peer-interactions. Teachers have expressed their concerns in the near-monotonous online classes with a Virtual Community. Lack of 'human' skills like empathy and communication are of paramount importance. Overall, it is found that the

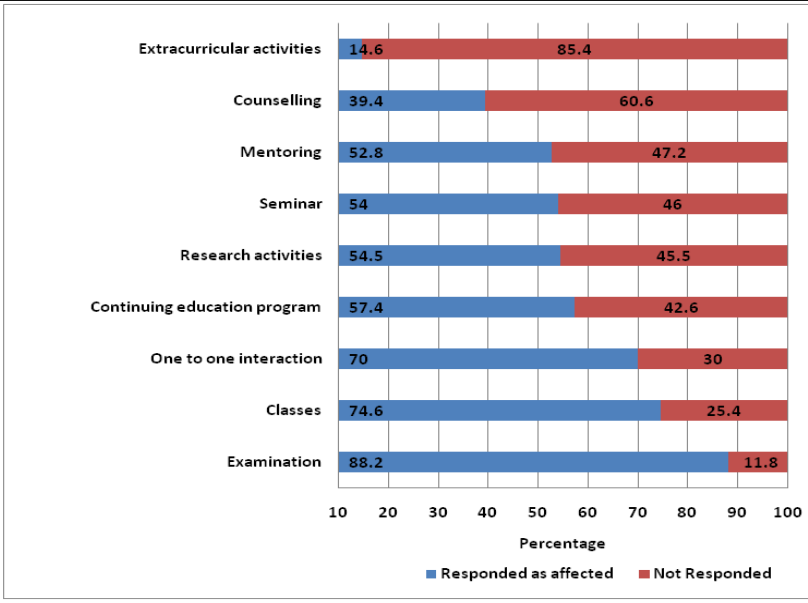

Fig 2 — Percentage Distribution of Health Science Faculty Members Participated In the Online Survey Based On Response Regarding the Academic Activities Affected by Lockdown

Fig 2 depicts that most of the (88.2%) faculty members participated in the survey responded as lockdown affected the examinations, 74.6% responded classes got affected, 70% responded as lost one to one interaction with students,colleagues and at the least 14.6% said extracurricular activities became affected.

Table 1 — *Percentage Distribution of Health Science Faculty Members and Students Participated in the Online Survey Based On Opinion Regarding Continuation of Online Class after* Lockdown

Participants	n1=3162 Frequency	Percentage (%)	n2=4044 Frequency	Percentage (%)
Faculty Members	1700	53.8	1462	46.2
Students	1375	34	2669	66

It is evident from Table 1 that, 53% of health science faculty members participated in online survey opinioned to continue online class after lockdown and 47% were not agreed upon continuation. At the same time, 34% of health science students participated in online survey opinioned to continue online class after lockdown and 66% were not agreed upon continuation.

human touch is lacking in online education. Conversion of hostels into quarantines is another factor which prevents outside students continuing their studies.

The worst affected is practical/clinical training. Lack of patients due to lockdown and fear of spread of the disease are the key elements. Staff cannot travel to the places of work.

Examinations in the KUHS pattern take the maximum brunt. Out-of-state examiners and out-of-zone examiners cannot report due to lack of travel facilities - air, road and rail. Indefinite postponement will disrupt the examination calendar prepared by the University.

Research has come to a near standstill. This is an area of great concern and should be addressed with earnestness.

(2) Financial : These are genuine concerns. Managements which barely thrive on the college alone might find the going tough. Already there are wage-cuts and employment layoffs in the news. There are also concerns that the online mode of teaching could result in lesser wages. Huge built-up areas are remaining un-utilized due to lockdowns, which, if continued, will accentuate the huge losses already accrued. Students and Teachers have expressed their concerns about the costs involved in the purchase of network time.

(3) Social : The insecurities created by COVID-19 are widespread and ubiquitous among all stakeholders. The availability of networks and the costs involved are areas of concern. This will enhance the digital divide. The quality of academic outcomes is affected. The parents of a few students, who were till now NRIs stationed in the UAE, expressed concerns over their ability to afford their wards' education in self-financing institutions.

On the contrary, there are positive outcomes also. Online teaching gave an opportunity to innovate and execute newer pathways for Health Care Education. It has benefited for both the staff and students.Working from Home as a modality has become the new norm. Thus online classes have brought a great opportunity for digital revolution in education and transformation in the role of a teacher. It is safe to presume that this section of students does not seem to face any issues when transitioning from a college to home environment. It is also equally important to assess the quality and effectiveness of the learning materials being provided to the students.

Possible Solutions

- It is necessary to explore digital learning, digital skill of the teachers and students need to be emphasized[6,7].
- Specialized Teaching Methodologies have to evolve for Online Teaching.
- Teachers and students need to be trained for this.
- Jobs and Salaries of Teachers should be protected.
- On Campus-off Campus Teaching Systems can be tried in future.
- Measures should be taken to mitigate the effect of the pandemic on Internship Program, Research Projects and Job offers [8].
- Integration of technology into Health Science Education like Simulation, Social Media should be actively explored.
- The Emotional Issues of Students in this scenario should be addressed[9,10].

Conclusion

The impact of COVID-19 is all encompassing and has shaken the World to its foundations. Its impact on Health Science Education Sector is similar to the damage every other is facing. But it is possible that, with some careful planning, we might be able to limit the long-term adverse consequences of this prolonged shutdown. Colleges need resources to rebuild the loss in learning, once they open again[10]. It is important to reconsider the current content delivery and pedagogical methods in colleges by seamlessly integrating classroom learning with e-Learning modes to build a unified learning system. The University should play a leadership role in these uncertain times to steer the ship in uncharted path. In this special circumstance, we need a well-rounded and effective educational practice for the capacity building of young minds. It will develop skills that will drive their employability,

productivity, health and well being in the decade to come and ensure the overall progress and leadership role Health Science Education Sector.

Limitations :

- The study was confined to small number of subjects in a State Level University, which limit the generalization.
- Google survey form was used to collect data due to National Lockdown. Other methods like Focus Group Discussions could not be used to gather in-depth data.

Conflict of Interests : Authors declare that they have no conflict of interest.

Ethical Issues : An online informed consent was taken from all participants during the study.

Financial Support : No external financial support received for this study.

Acknowledgement : The authors are grateful to the faculty members of affiliated Institutions under Kerala University of Health Science for the participation in the study.

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Original Article

A Correlation Study between Red Cell Distribution Width and Ranson Score in Predicting Severity and Outcome of Acute Pancreatitis

Rupak Protim Patir[1], Rimamoni Doley[2], Anup Kumar Das[3]

Introduction : Some patients with Acute Pancreatitis develops severe feature and it accounts for 20% of patients with Acute Pancreatitis. Our study is conducted with an aim to investigate the correlation between Red Cell Distribution Width and Ranson score in patients with Acute Pancreatitis.

Methods : 119 patients suffering from Acute Pancreatitis were studied and they were divided into 2 groups - patients with Mild or Severe Acute Pancreatitis according to the presence or absence of the features of organ failure for >48 hours and/or local complications. Routine laboratory investigations, including complete hemogram and Red Cell Distribution Width, Liver Function Test (LFT), Renal Function Test (RFT), Serum Calcium, Serum Amylase, Serum Lipase, Serum Lactate Dehydrogenase (LDH), Serum Electrolytes, Arterial Blood Gas analysis, Ultrasonography of abdomen, Chest X-ray, Contrast Enhanced Computed Tomography (CECT) of whole abdomen were done. The data was tabulated and analyzed. Chi square test was applied to calculate the significance and p-value <0.05 is significant. The correlation between Red Cell Distribution Width – Co-efficient of variation and Ranson score was measured by using Pearson's correlation coefficient (r).

Results : 30 patients (25.21%) had features of severe type of acute pancreatitis. The cut-off values for Ranson score and Red Cell Distribution Width level in severe type of acute pancreatitis were ≥3 and 14.6% respectively. At time of admission, Red Cell Distribution Width correlated with Ranson score at 48-hour ('r' value of 0.7812 and 'p' value of <0.001).

Conclusion : Red Cell Distribution Width emerges as an independent prognostic factor in predicting severity and outcome of the acute pancreatitis patients.

[*J Indian Med Assoc* 2021; **119(10):** 22-5]

***Key words* : Acute pancreatitis, Red Cell Distribution Width (RDW), Ranson score; Severity.**

The inflammation of pancreas in Acute Pancreatitis (AP) is a reversible process and it can involve the peri-pancreatic tissue of other regional tissues or remote organ systems in varying degree[1]. The activation of pancreatic enzyme during AP causes pancreatic tissue damage and it results in an acute inflammation of pancreas, that has variable aetiology and natural histories, and making it difficult in the early identification of patients at high risk. 80% of AP cases are mild and has self-limiting course without sequelae. 10%-20% of cases develop severe disease and various parts of the pancreas and surrounding tissues become necrotic. The acute inflammation may lead to Systemic Inflammatory Response Syndrome (SIRS) and/or Multiorgan Failure (MOF) and results in death[2,3]. It is one of the most common gastrointestinal causes of hospital admissions in India and worldwide[4,5]. The incidence rate for AP is about 5-35/100,000 new cases annually worldwide[6] but the rate of mortality is currently approximately 3.8% to 7% as reported by several recent studies and in severe AP, it ranges from 7% to 42%[7,8].

Editor's Comment :

- RDW is a simple and easy tool for predicting the severity of the disease process and risk stratification in AP.
- An early, aggressive and effective treatment can be initiated in AP by this simple tool. Thus local and systemic complications and mortality in AP can be minimised.

In order to decrease mortality rates in AP, early identification of patients at greater risk of mortality may be determined by rational use of diagnostic studies and prompt early institutional or medical intervention. In previous studies, the use of several biological markers and clinical events has predicted the mortality of AP. But, there has been a search for a tool for a reliable risk stratification to predict the severity and prognosis of AP. The variability in the size of circulating erythrocytesis measured quantitatively in RDW and the higher value of RDW reflects the greater heterogeneity in cell sizes (ie, anisocytosis). RDW is a routine and inexpensive test that can be obtained through a complete blood count which is easily

Department of Medicine, Assam Medical College and Hospital, Dibrugarh 786002
[1]MBBS, Postgraduate Trainee and Corresponding Author
[2]MBBS, MD, Assistant Professor
[3]MBBS, MD, Professor

Received on : 23/09/2020
Accepted on : 03/11/2020

available. It is calculated[7] as –

$$RDW = \frac{(\text{Histogram Width of 68.26\% of RBC}) \times 100}{\text{Mean Corpuscular Volume (MCV)}}$$

For these reasons, recent studies have focused on RDW to predict the severity and mortality in AP. The mortality in AP patients can be reduced by early diagnosis in the Emergency Department and prompt treatment. Therefore, the simple, easily accessible and affordable markers are needed which allows investigation at the bedside to assess whether the disease will progress in severity and predict development of complications and mortality, without any delay. There has been limited numbers of studies about the correlation of RDW with severity of AP. Hence, further studies examining the possible prognostic value of RDW for predicting various outcomes related to AP are still warranted.

Aim and Objective

The study was conducted to correlate and evaluate the outcome of AP by Ranson's criteria and RDW.

Materials and Methods

It was a cross sectional study done between 1st July, 2018 to 30th June, 2019. All consecutive patients presenting with typical signs and symptoms of AP, admitted in our hospital were taken up for the study after fulfilling the selection criteria. A total of 119 patients of Acute Pancreatitis were included in the present study. Inclusion criteria included- age >12 years old, all cases of AP and those who gave consent for the study. Exclusion criteria included- age ≤12 years old, anaemia, chronic kidney disease, chronic liver disease, cancer patients, pregnancy and recent history of blood transfusion within 3 months.

The diagnosis of AP (according to revised Atlanta classification)[9] required any two of the three features – (i) pain abdomen consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back); (ii) raised serum lipase or amylase activity (≥ thrice the upper limit of normal); and (iii) characteristic features of AP on Contrast-enhanced Computed Tomography (CECT), Magnetic Resonance Imaging (MRI) or Transabdominal Ultrasonography.

AP was classified into 2 groups - as Mild Acute Pancreatitis (MAP) and Severe Acute Pancreatitis (SAP) based on the presence/absence of organ failure for >48hours and/or local complications.The organ failures included Systolic Blood Pressure (SBP)<90 mmHg (shock), pulmonary insufficiency (SpO_2<90%) and renal failure (serum creatinine level >2 mg/dl). Local complications included acute peri-pancreatic fluid collection, pseudocyst of pancreas, acute necrotic collection and walled-off necrosis.

Demographic profile was collected from patients. Routine laboratory investigations, including complete hemogram and RDW, Liver Function Test (LFT), Renal Function Test(RFT), Serum Calcium, Serum Amylase, Serum Lipase, Serum Lactate Dehydrogenase (LDH), Serum Electrolytes, Arterial Blood Gas analysis (ABG), Ultrasonography (USG) of abdomen, Chest X-ray (CXR), Contrast Enhanced Computed Tomography (CECT) of whole abdomen were done.

At the time of hospital admission, RDW was calculated. From the data recorded in first 24 hours and 48 hours after admission, Ranson score was calculated. Patients with Ranson score ≥3 had the severe disease (SAP).

Statistical Analysis :

The data recorded on pre-designed and pre-tested proforma was tabulated and master chart was prepared. Applicable statistical methods were used to analyse the various sets of data by using a computer program Statistical Package for Social Sciences (SPSS for Windows, Version 21.0. Chicago, SPSS Inc). The discrete data were expressed as proportion and percentage and were analysed by using Chi square test. Significant P-value was <0.05.The correlation between Red Cell Distribution Width – Co-efficient of variation (RDW-CV) and Ranson score was measured by using Pearson's correlation coefficient (r).

Results

In our present study, all the patients belonged to the age group of 13 to 71 years with mean age of 36.37 ± 10.85 years. Other demographic features were shown in Table 1.

The mean RDW for MAP was 13.92±0.84 while that of SAPwas 16.43±1.41. It was observed that out of total 70 patients with RDW-CV level in the range of 11.6-14.6%, SAP and mortality were seen in 1 and 0 patients respectively. However, out of total 49 cases with RDW-CV level in the range of >14.6%, SAP and mortality were seen in 29 and 15 patients respectively (Table 2).

Out of total 76 patients with Ranson score <3, no mortality was observed among the patients and no patients had developed severe acute pancreatitis. However, out of total 43 patients with Ranson score ≥3, 30 patients had developed SAP and death had occurred in 15 patients (Tables 3 & 4 and Fig 1).

In the above figure, a positive correlation between RDW at time of admission and Ranson score with a 'r' value of 0.7812 and significant 'p' value (p-value <0.001) was seen.

Table 1 — *Demographic and Clinical Characteristics of the patients with AP*

Characteristics	Total (n=119)	Patients with MAP (n=89)	Patients with SAP (n=30)
Sex :			
Male	102	74	28
Female	17	15	2
Aetiology :			
Alcoholic	83	58	25
Gallstones	27	24	3
Idiopathic	18	18	0
Hypertriglyceridemia	3	1	2
Mean hospital stay (in days)	5.5	4.72±1.14	7.63±2.29
Mean RDW	14.55±1.49	13.92±0.84	16.43±1.41
Mean Ranson score	1.91±1.85	1.07±1.07	4.40±1.38
Outcome :			
Improved	104	89	15
Expired	15	0	15

Discussion

In our study, there was a positive correlation between RDW and Ranson score with a significant difference in RDW between MAP and SAP.

In our study, it was seen that patient with higher Ranson score (≥3) had more complications and mortality with sensitivity of 40% to 80%. It became the common and simple scoring systemto evaluate severity of AP. Ranson score was used as important tool in predicting the patient's outcome in AP in the studies of Khanna A K *et al*[10]and Chand *et al*[11].

RDW was an independent prognostic marker to determine risk of complications and mortality in varied range of clinical manifestations. Senol *et al*[7] observed in their study that patients with severe AP had increased RDW values (cut-off of 14.8%). Peng Tao *et al*[12] found in their study that RDW was an independent risk factor for persistent organ failure (Hazard ratio 2.26, 95% confidence interval: 1.46-3.51; P<0.001) after uni-and multi-variable analysis. The best cut-off value of RDW was 13.05% to predict the persistent organ failure with an area under the curve of 0.791 with a sensitivity of 97.4% and specificity of 55.8%. Zhang Ting *et al*[13] also found significantly higher RDW values in patients with moderately severe acute pancreatitis and severe acute pancreatitis (14.03±1.74% *versus* 13.23±1.23%, P<0.001) in comparison to mild acute pancreatitis in their study. Moharamzadeh *et al*[14] found in their study that the mean RDW of the patients was 13.82±1.69%. Mean RDW in dead patients and other patients was 16.44±4.22% and 13.68±1.37% respectively (P<0.001). The cut-off point of 14.55% for RDW with 80% sensitivity and 85% specificity was determined for predicting mortality in patients. In our study, it was seen that patients with higher RDW-CV level (SAP 16.43±1.41% *versus* MAP 13.92±0.84%) had higher proportion of SAP and mortality. Also, it was observed that out of total 70 patients with RDW-CV level in the range of 11.6-14.6%, SAP and mortality were seen in 1 and 0 patients respectively. However, out of total 49 cases with RDW-CV level in the range of >14.6%, SAP and mortality were seen in 29 and 15 patients respectively.

Kilic *et al*[15] observed that RDW (14%) at time of hospital admission was correlated with Ranson score ≥4 at 48-hour after admission (r=0.22; p<0.002). In our study, it was observed that RDW at time of hospital admission (14.6%) was correlated with Ranson's score ≥3 in predicting SAP and mortality than novel prognostic markers in the literature used to predict mortality ('r' value of 0.7812 and 'p' value of <0.001). In our study, sensitivity and specificity of RDW in diagnosis of SAP was 83.7% and 82.89% respectively

Table 2 — *Distribution of patients with RDW*

RDW–CV Level (%)	Number (n=119)	Mild Acute Pancreatitis		Severe Acute Pancreatitis		Mortality	
		n	%	n	%	N	%
11.6–13.6	34	34	100.00	0	0.00	0	0.00
>13.6–14.6	36	35	97.22	1	2.78	0	0.00
>14.6–15.6	23	18	78.26	5	21.74	0	0.00
>15.6–16.6	15	2	13.33	13	86.67	4	26.67
>16.6	11	0	0.00	11	100.00	11	100
Total	119	89	74.79	30	25.21	15	12.61

Table 3 — *Distribution of patients with Ranson score*

Ranson's Score	Number (n=119)	Mild Acute Pancreatitis		Severe Acute Pancreatitis		Mortality	
		n	%	n	%	N	%
0–2	76	76	100.00	0	0.00	0	0.00
3–4	32	13	40.63	19	59.38	5	15.63
5–6	8	0	0.00	8	100.00	7	87.50
≥7	3	0	0.00	3	100.00	3	100.00
Total	119	89	74.79	30	25.21	15	12.61

Table 4 — *Association between RDW and Ranson score*

RDW–CV Level (%)	Number (n=119)	Ranson's Score <3		Ranson's Score ≥3		P-value
		n	%	n	%	
<14.6	70	63	90.00	7	10.00	<0.001
>14.6	49	13	26.53	36	73.47	
Total	119	76	63.87	43	36.13	

with a negative predictive value of 90%.

Our findings also support the useful role of RDW as a quick and easy method for risk assessment in AP.

Conclusion

RDW level at the time of hospital admission is helpful to predict the severity of AP in the earliest time, especially at first-line centres, as compared to the multifactorial complex scoring systems presently available. After evaluation of the cases, it was observed that AP patients with higher RDW level were at greater risk for developing severity as well as mortality. Importantly it was also observed that RDW was a better predictor for severe disease and mortality than Ranson score. Therefore, in our setup, RDW should be assessed in all patients suffering from acute pancreatitis to help in early risk stratification, thus guiding the initiation of early, aggressive and effective treatment and prevention of both local and systemic complications as compared to standard Ranson criteria that takes longer period of assessment.

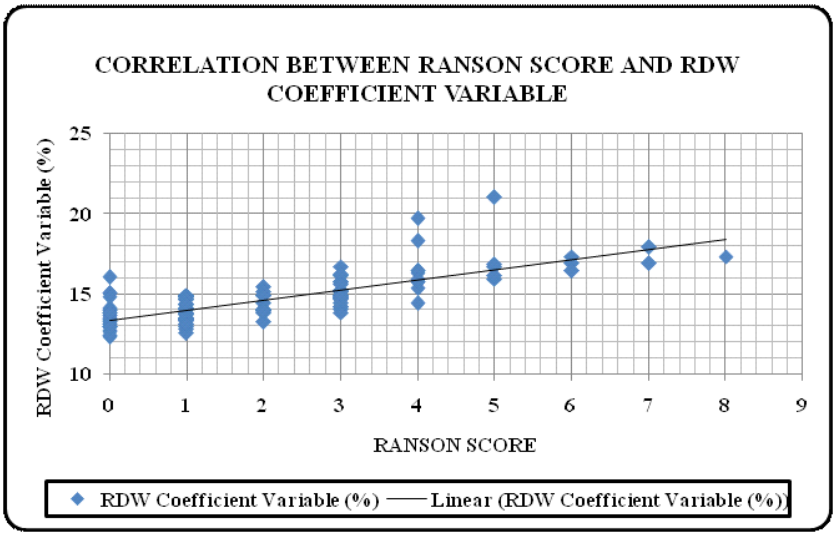

Fig 1 — Correlation between RDW with Ranson score

Limitations :

(1) More cases needed.

(2) Validation studies needed in future homogenous cohorts.

Financial Support : None

Conflict of interest : None

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Original Article

Ambulatory Blood Pressure Monitoring for Ideal Blood Pressure Controll : A Kenyan Retrospective Review

Anthony Gikonyo[1], Caroline Irungu[2], David Kanyeki[2], Stephen Omondi[2], Ruot Teny[2], Mikhail Basem[3], Boniface Musila[2], Erica Cimpaye[2], Lamin Jeitah[2], Premanand Ponoth[4], Dan Gikonyo[5]

Ambulatory Blood Pressure Monitoring is a useful tool for the diagnosis and monitoring of hypertension. Its use is limited due to both access to the technology and financial constraints. We present our limited experience with it to expound on its strengths and utility. We had a total of 30 studies performed between November, 2018 to August, 2019. There were 26 patients with a diagnosis of hypertension,17 on medication and 9 not on medication. 16 tests achieved the greater than 70 % required percentage of readings over 24 hours. The results showed that of the hypertensive patients with elevated office blood pressure were controlled by ambulatory blood pressure guidelines. More research is required to understand the full potential of ambulatory blood pressure monitoring to assess control of blood pressure.

[*J Indian Med Assoc* 2021; **119(10):** 26-8]

Key words **: Ambulatory Blood Pressure, Hypertension, ABPM.**

The high initial cost of Ambulatory Blood Pressure Monitoring (ABPM) devices has precluded their widespread use in low income settings in Sub-Saharan Africa. There is little information to assess the potential clinical and public health benefits of ABPM in such settings[1]. Owing to the relative availability and ease of use, office BP measurement is commonly used for the assessment of BP control in patients but over the last decade, several studies have shown that out-of-office BP measurements perform better and ABPM is recognized as the gold standard[2].

High prevalence of white coat hypertension existed among participants studied. Hence, ABPM should be included as part of routine work-up for newly-diagnosed hypertensive patients in order to limit the number of those who may be committed to lifelong anti-hypertensive medications with its unwanted side effects[3].

Material and Methods

We had a total of 30 studies performed between November, 2018 to August, 2019. There were 26 patients with a diagnosis of hypertension, 17 on medication and 9 not on medication. 16 tests achieved the greater than 70 % required percentage of readings over 24 hours.

Editor's Comment :

- Blood pressure monitoring out of hospital required to achieve target blood pressures.
- In addition to home blood pressure monitoring, ambulatory blood pressure monitoring is an essential tool to confirm appropriate blood pressure control.
- It's greater availability and utilization will improve patient care.

ABPM provides the average of blood pressure readings over a defined period, usually 24 hours. The device is typically programmed to record BP at 15–30 min intervals, and average blood pressure values are usually provided for daytime, nighttime and 24 hours. A minimum of 70% usable BP recordings are required for a valid ABPM measurement session. The diagnostic threshold for hypertension is at least 130/80 mmHg over 24 hours at least 135/85 mmHg for the daytime average and at least 120/70 for the nighttime average[4].

We collected ABPM data over a period of 12 months. The majority of patients were either undergoing the test to confirm a diagnosis of hypertension or were hypertensive and determining blood pressure or possible white coat hypertension. There were 30 tests performed, each preceded by an office blood pressure for comparison. Each participant was monitored for 24 hours.

Results

Only 16 of the 30 tests were valid based on the

Department of Cardiac Sciences, The Karen Hospital, Nairobi, Kenya.
[1]MRCP, FACC and Corresponding Author
[2]MbChb, M Med
[3]MbChb, Msc
[4]MS, Mch, FACS, FACC, FICS, FIACS, FACP
[5]MbChb, M Med, FACC

Received on : 06/03/2021
Accepted on : 08/05/2021

70% criteria. There were 26 patients with a diagnosis of hypertension, of these 9 were not on medication and required a confirmation of the diagnosis. There were 17 patients with hypertension on medication who required to ascertain control of the blood pressure (Table 1).

The results as seen on Table 2, illustrated that of the 17 hypertensive patients with elevated office blood pressure on medication only 2 were controlled on based on ABPM analysis. The 9 patients not on medication with a diagnosis of hypertension, 7 were either normotensive or had borderline diastolic blood pressures.

Table 1 — *Demographic data and results of ABPM*

Gender	Age	Diagnosis	Office Blood Pressure	Number of Total Measurement Overall	% Succeed Overall	Average Overall	Average Awake (mmhg)	Average A Sleep (mmhg)	Dipper (Yes/No)
F	38	HTN	146/102	29	51	115/82	115/82	0/0	
F	37	NO	128/70	44	81	115/75	117/76	105/67	NO
F	51	HTN	140/80	32	68	115/78	116/79	113/74	NO
F	36	HTN	120/71	41	85	137/96	142/99	122/85	NO
M	59	HTN	141/79	29	63	136/79	138/79	125/76	NO
F	47	NO	90/85	87	63	135/89	136/90	130/82	NO
M	60	HTN	145/98	34	59	128/79	127/79	132/77	NO
M	59	HTN	131/81	36	78	120/83	122/86	112/86	NO
M	59	HTN	145/90	43	14	138/99	140/101	127/91	NO
F	70	HTN	170/110	22	24	130/85	130/84	132/86	NO
F	43	HTN	120/66	42	91	142/94	142/96	139/86	NO
F	69	HTN	119/78	22	46	131/87	135/91	121/77	NO
M	35	HTN	145/83	32	64	139/95	143/98	126/87	NO
F	31	HTN	135/98	30	70	125/84	125/86	126/77	NO
F	78	HTN	168/71	42	89	135/78	135/78	137/76	NO
F	30	HTN	142/99	29	69	120/83	125/87	107/73	NO
M	48	HTN	149/89	40	83	126/86	128/88	118/79	NO
M	46	HTN	143/93	43	93	122/86	121/87	124/81	NO
M	32	HTN	154/114	41	87	132/96	134/96	125/94	NO
M	43	HTN	158/125	43	96	131/98	132/100	127/91	NO
M	52	HTN	141/102	24	56	123/86	130/91	110/78	YES
F	22	HTN	141/93	33	73	122/81	124/84	115/72	NO
M	37	HTN	150/87	37	97	127/82	129/82	121/79	NO
F	52	HTN	169/96	34	85	140/95	141/96	136/93	NO
M	51	HTN		34	74	134/92	139/96	120/81	NO
F	66	HTN	169/92	37	22	139/75	142/78	129/64	NO
F	48	NO		42	91	108/72	110/74	101/64	NO
F	47	HTN	152/71	28	57	112/72	116/77	105/61	NO
M	32	NO	125/72	33	67	110/73	111/74	106/69	NO
M	46	HTN	167/115	43	93	138/92	141/93	127/87	NO

Discussion

Screening blood pressure measurement significantly overestimated hypertension prevalence while failing to identify approximately 50% of true hypertension diagnosed by ABPM[1]. Rates of hypertension were significantly lower when measured by 24-hours ABPM (55.7%) than by office blood pressure measurement (78.4%). White coat hypertension was observed in 54 participants (68.4%)[5]. This is reflected in our data with only 2 of the 9 patients being screened based on elevated office blood pressure being hypertensive. This may indicate that we may be overestimating the

Table 2 — *Patients with hypertension on medication comparing office and ambulatory blood pressure measurements*

Medication	Office blood pressure	Ambulatory blood Pressure
Bisoprolol	146/102	115/82
Verapamil	140/80	115/78
Methyldopa	120/71	137/96
Amlodipine, Losartan	141/79	136/79
Amlodipine, Bisoprolol, Ibersartan, Methyldopa, Eplerenone	145/98	128/79
Telmisartan, Amlodipine	131/81	120/83
Telmisartan, Amlodipine, Bisoprolol	145/90	138/99
Amlodipine, Losartan, Hydrochlorothiazide	170/110	130/85
Amlodipine	120/66	142/94
Valsartan, Hydrochlorothiazide, Spironolactone	119/78	131/87
Bisoprolol, Spironolactone	168/71	135/78
Losartan	142/99	120/83
Telmisartan, Amlodipine, Nebivolol, Spironolactone	158/125	131/98
Amlodipine, Nebivolol, Hydralazine, Ibersartan	169/96	140/95
Bisoprolol		134/92
Losartan, Spironolactone	169/92	139/75
Telmisartan, Amlodipine, Spironolactone, Nebivolol	167/115	138/92

actual disease burden based on only office blood pressure measurements. In addition, there was suboptimal blood pressure control of patients already on medication based on the ambulatory blood pressure results. This was partially driven by the average diastolic cut off being 80mmHg.

Conclusion

More research is required to understand the full potential of ABPM to assess control of blood pressure.

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Original Article

Xanthogranulomatous Cholecystitis, A Paradox in Diagnosis & Treatment : A Case Series

Mriganka Ghosh[1], Soumita Ghosh Sengupta[2]

Xanthogranulomatous Cholecystitis (XGC) is an enigmatic variation of Gall Bladder inflammation. Its incidence varies from 0·7% to 10% cumulatively with definite preponderance in India and in far East Countries. Because of its extensive inflammation of varying proportion unmatched with clinical presentation, surgeon more often encounters trouble ended up doing overzealous surgery and histopathology comes as relief or disappointment.

We encountered few cases of XGC during last 1 and half years in Medical College, Kolkata and analysed them retrospectively and came up with some interesting observations.

In our small yet significant case series, we were fortunate enough to experience multiplex presentations of XGC giving impression of both Cholelithiasisand carcinoma mainly during surgery planned for Cholecystectomy. There are few distinctive CT scan findings segregating XGC from carcinoma but they are yet to be authoritative. Other modalities of superior imaging also are not much encouraging. Only and best option is routine use of peroperative Frozen section.

Conclusion : Thanks to its peculiarity yet similarities with both benign and malignant disease, XGC remains to be an disturbing element for the surgeons till any algorithmic approach helped by pre-operative radiology and others comes in the horizon.

[*J Indian Med Assoc* 2021; **119(10):** 29-35]

Key words **: Xanthogranulomatous Cholecystitis, Gall Bladder carcinoma. Frozen section.**

Xanthogranulomatous Cholecystitis (XGC) is an enigma. Although for surgeons it is a known entity but the existence of this is repeatedly forgotten till the very histopathological diagnosis comes as a surprise and as a reminder[1,2]. Then, either this unanticipated diagnosis gives a sigh of relief to the patient, relatives and also to the treating surgeon when the possibility of carcinoma is looming large. Or it could be a source of disappointment when already performed radical surgery appeared as an unnecessary exercise.

The reason is although a separate entity, its clinical presentations are nothing indistinguishable from those of different spectrum of Cholelithiasis[3,4]. Rarely it may present with obstructive Jaundice or with diffuse wall thickening in Contrast Enhanced Computed Tomography (CECT) when the suspicion wavers between choledocolithiasis, Mirizzi syndrome and more sinister Gall Bladder Carcinoma (GBC) but unfortunately the thought of XGC remains elusive till the Histopathology Report (HPE) comes. This downside of this missed diagnosis is either overtreatment or undertreatment[5-7].

Editor's Comment :

- Although Xanthogranulomatous Cholecystitis will continue to create diagnostic dilemma and mixed emotion after surgery and HPE, focused radiology and then liberal frozen section still can win us considerable success.

Hence there needs to be an increased awareness of this tumour mimic, particularly in endemic areas like India[1,2]. Identifying the preoperative differences (either clinically or radiologically) between XGC and GBC is imperative, as it would help avert unnecessary morbidity especially in the form of radical surgery. Numerous study were done to search for the CT findings suggesting XGC and few algorithm were made for its early suspicion but they are yet to be of some value in larger scale.

We went through the preserved database of patients operated-upon with a pre-operative diagnosis of calculous cholecystitis with or without suspicion of Gall Bladder Carcinoma (GBC) in the Department of General Surgery of Medical College, Kolkata catering a large number people hailing from either side of river Ganga, the so-called endemic zone for GBC, between January, 2019 and December, 2020 and looked for those cases which eventually demanded more than what was planned. Either it is mere conversion from lap to open or more extensive multi visceral surgery. Of them, we segregated those cases whose final HPE revealed

[1]MBBS, MS(General Surgery), Associate Professor, Department of General Surgery, Medical College and Hospital, Kolkata 700073

[2]MBBS, MD(Pathology), Associate Professor, Department of Pathology, College of Medicine & Sagore Dutta Hospital, Kolkata 700058 and Corresponding Author

Received on : 15/02/2021
Accepted on : 17/02/2021

Xanthogranulomatous Cholecystitis (XGC) and analysed them in terms of symptoms, signs, laboratory data, operative findings and postoperative progress and found some interesting things which are worth sharing.

Case 1 :

A male patient of 50 came to surgery out patient department with dark yellow urine, eyes and generalised body surface for two months with occasional mild pain in upper abdomen associated with loss of appetite. The Jaundice was progressive in nature. There was no history of (H/O)associated nausea and vomiting, significant weight loss, blood vomiting and black stool or bleeding per rectum. General survey revealed only deep Jaundice and systemic local examination was unremarkable.

The blood picture showed interesting progression of Jaundice. His Liver Function Test (LFT) showed typical picture of obstructive Jaundice ; initially total bilirubin was 6.9 mg/dl (conjugated fraction was 5.5mg/dl) which rapidly progressed to 17.7mg within 3 weeks. The finding of triphasic CT scan (Fig 1),as advised with the suspicion of malignant aetiology, was equivocal showing contracted Gall Bladder with diffuse wall thickening and loss of fat plane at places. CA 19-19 level in blood was within normal range. Meanwhile, another LFT report after 2 weeks showed an interesting change, ie, diminution of total and conjugated bilirubin.

An exploratory Laparotomy was planned with keeping option of per operative Frozen Section. There was a conglomerated mass in the Liver bed, containing part of transverse Colon, Duodenum and Stomach burying the GB inside. The adhesion appeared dense but separable and with painstaking dissection, the Gall Bladder was separated from the rest, pus aspirated from within and Cholecystectomy was done. The specimen was sent to pathology department and its frozen section soon revealed Xanthogranulomatous Cholecystitis. We closed the abdomen after all form of haemostasis and placing a drain inside.

Case 2 :

A male case of calculous cholecystitis was planned for Laparoscopic Cholecystectomy. The relevant history is an episode of acute cholecystitis which needed hospitalisation and conservative management. During interval cholecystectomy, gross adhesions between Gall Bladder with the adjacent organs was noted and a suspected duodenal injury during an attempt to separate GB from duodenum prompted us to convert. On conversion and on attaining further clarity, the Gall Bladder was separated from adjacent viscera. It was thick walled, grossly inflammed and

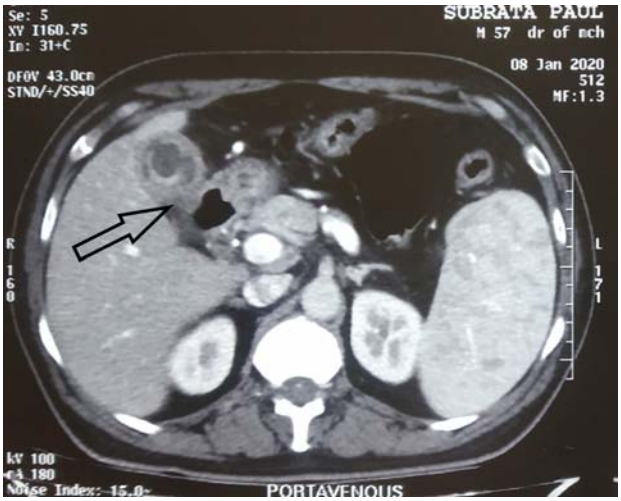

Fig 1 — Showing finding of triphasic CT scan

there was stony hardness at the neck probably due to impacted large stone. Cholecystostomy was done to express out multiple small calculi but hardness at the neck was not due large impacted stone but due to a homogeneous mass at the neck, almost completely obliterating the lumen. There was no apparent lymphadenopathy elsewhere. Partial cholecystectomy with removal of part of GB bearing the suspicious mass and leaving a stump of 1cm length was completed. The leak at the second part of duodenum was repaired. But postoperative drain collection was bilious and unusually high and CECT revealed intact duodenum. An MRCP showed a leak at proximal part of extrahepatic bile duct. ERCP was required to put a stent beyond the leak. Drain collection soon became minimal, patient tolerated semisolid diet well. No further definitive radical surgery, as anticipated was required as HPE revealed XGC.

Case 3 :

The next case was a 76 years old female with H/O of vague upper abdominal pain, vomiting off and on for a duration of 1 month, her abdominal sonography (USG) showed cholelithiasis with thick GB wall. To evaluate further, triphasic CT and MRCP followed. CT abdomen revealed thick walled distended GB but fat plain between GB liver maintained, suspicious lymph nodes at porta, while in MRCP ,CBD was found mildly dilated. A 3.5 mm filling defect within CBD warranted Endoscopic Retrograde Cholangiopancreatography (ERCP), followed by sphincterotomy and Endoscopic Papillary Balloon Dilatation (EPBD).

An open exploration with Frozen Section facility was planned in anticipation difficult surgery and suspicious pathology. A conglomerated mass as discovered demanded extensive adhesionolysis to

segregate grossly distended, very thick walled GB with calculus impacted at the neck from the adjacent viscera eg, the omentum, transverse Colon, Stomach and Duodenum all appeared to be part of gross inflammatory process . Lymph nodes at lesser omentum and hepatoduodenal ligaments (LN 8,12,13) were found enlarged, but there was no ascites or metastasis in liver bed or elsewhere. After cholecystectomy, the GB was cut open to reveal 3 suspicious areas of fatty infiltration, two in body & one in neck. As Frozen biopsy commented only suspicious pathology without any definitive conclusion, surgery was further advanced to removal of liver bed and clearance of lymph nodal basin. Final HPE gave a diagnosis of acute on chronic cholecystitis with xanthomatous changes with no evidence of malignancy in any part of specimen.

Case 4 :

Sonology of a 46 years male patient with pain upper abdomen, being investigated for suspected cholelithiasis, came as a surprise as USG detected thickened and irregular GB wall along multiple calculi, with indistinct fat plane between GB and liver. Suggestion was of CA GB with contiguous extension to Liver.

CT substantiated the USG findings, but also added that the diffusely thickened wall was irregular and appeared discontinuous at places (Fig 2). Fat planes between Liver and GB fundus were indistinct. No metastasis seen. No definite diagnosis was given. CA 19-9 was raised.

Extended cholecystectomy with removal of hepatoduodenal lymph nodes. GB specimen showed impacted large stone at the neck.

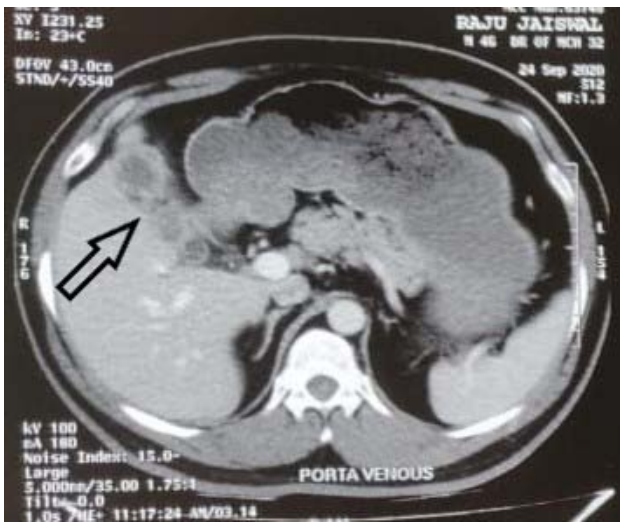

Fig 2 — Showing CT substantiated the USG findings

Second surprise came in the form of HPE which was compatible with XGC with no feature of malignancy. Lymph nodes were reactive.

Case 5 :

Next case is a female patient of 50 with H/O pain abdomen, single bout of melaena ,anorexia and weight loss in last 2-3months.USG revealed GB calculus with irregular thickening of GB wall at fundus. MDCT showed irregular wall thickening at fundus of GB and an oval lesion in the lumen in body region measuring 2.2 x 1.5 cm. There was significant lymphadenopathy in and around porta. In open surgery, the GB was distended, thickening of wall was obvious at fundus. Cholecystectomy was completed and the specimen was readily sent for Frozen Section which reported inconclusively with no suggestion of malignancy. The liver bed of 2 cm margin and few suspicious lymph nodes were removed. HPE came as XGC.

Case 6 :

A planned laparoscopic cholecystectomy was soon converted for difficult anatomy with transverse colon seen occupying the Liver Bed burying the GB underneath. Any attempt to separate and pull the colon up was thought to be beset with danger of colonic injury. On conversion, the overlying part of transverse colon was pulled up carefully from underlying GB, which was small, contracted and part of it seen densely adhered to colon and to structures in the lesser omentum. The part of colon, adhered to GB was suspiciously thickened but rest were apparently okay. At a point of dissection, proximal CBD got injured while separating the GB from it . As there was no provision of frozen section, a multivisceral surgery had to be done in suspicion of malignancy (primary source is either GB or colon) with radical cholecystectomy and hepatico jejunostomy and transverse colectomy and colo-colic anastomosis. The postoperative period was expectedly eventful but patient recovered well, tolerated semi solid in due time and was discharged eventually. The HPE report of GB specimen was of XGC while the suspicious part of transverse colon revealed nonspecific fibrosis. There was no evidence of malignancy.

Case 7 (7A,7B,7C) :

Three female cases had almost similar course of disease and similar per-operative findings and outcome. All were operated in three separate occasions for the diagnosis of cholelithiasis, no H/O acute attack and hospitalization, slated for lap surgery, had to be converted into open surgery because of considerable adhesions and suspected CBD injury.

Two had partial right lateral wall tear while the other one had complete transection of CBD just distal to hilum. Roux-en-Y hepatico jejunostomy (side to side and end to side respectively) along with cholecystectomy was done .In all cases ,the HPE were XGC (Table 1).

Discussion

Xanthogranulomatous Cholecystitis (XGC) is a chronic inflammatory disease of the Gall Bladder characterized by focal or diffuse destructive inflammation with marked proliferative fibrosis along with infiltration of macrophages and foamy cells[5,7]. Surgeons encounter them off and on either in operating theatre or when the HPE report comes to hand. Latter is the commonest. Its incidence ranges from 0.7 to 10%[5,7,8]. Ofcourse, the incidence wise, marked geographical and ethnic variations were obvious in past studies.

In the largest European series to date together with all previously published series in order to gain a worldwide perspective of XGC, 42 (0.9%) were diagnosed as XGC on pathological review out of 4773 cholecystectomies performed at SJUH during the study period[9]. Rather, the cumulative data from India histopathology a far East and America revealed overall incidence of XGC 1.3-1.9%, with the exception of India where it was 8.8% and incidence of GBCa is higher in Indian and Far Eastern populations than in Western populations. There were no patients with XGC associated with GBCa[9].

The male-to-female ratio appears to be equal with little geographical influence although, Indian study reflected a female preponderance in more than one occasion.

The pathogenesis is speculative but reported opinions mostly favoured stasis being the common final pathway, which results increased intra GB pressure, ruptured Aschoff's sinuses, formation bile lake and a final intense inflammatory response to this extravasated bile[10-12]. Occasional wall dehiscence results fistulisation. The association of Gall Bladder Ca with XGC makes the scenario further complicated.

Talking of Indian perspective, Vinodh Dixit *et al* in their study,the so called first study over XGC way back in 1993 reported a surprising incidence of 9.34% among

Table 1 — *All cases with pre-operative and intraoperative findings with final HPE of XGC*

	Any clue	CT Finding	Open/Lap	Frozen, If asked	Operative	Iatrogenic Injury	Excess Surgery/ hazards	HPE
					Adh / Mass / Fistula			
1	Jaundice	Diffusely thick W/FP lost at places	Open	Yes Finding-XGC	Mass of GB/ colon/duodenum			XGC
2	Nil	Not done	Converted	No	Thick Wall GB, Hardness at Neck, Cholecysto-duodenal fistula	Duodenal & CBD (missed)	Duodenal Repair ERCP & Stenting	XGC
3	USG	Thick wall GB, Nodes at porta		Yes Inconclusive	Thick wall GB, Conglomerated mass/nodes		Extended Choli Nodal Clearance	XGC
4	USG	Thick, irregular wall with discontinuity at places	Open	No	Simulates GBC		Do	XGC
5	USG	Thick irregular fundus/Nodes at porta	Open	Yes inconclusive	Thick fundus, Oval lesion in body		Liver bed excision/ Nodal Clearance	XGC
6	Nil	Not done	Converted	No	Mass with Cholecysto-Colic fistula	CBD	Rad Choli+ HJ+ Tr-colectomy	XGC
7A	Nil	Not done	Converted		Gross Adhesion	CBD,lat wall	HJ	XGC
7B	Nil	Not done	Converted		Do	CBD,lat wall	HJ	XGC
7C	Nil	Not done	Converted		Do	CBD transection	HJ	XGC

routine cholecystectomy specimens[13]. By then,no parallel series existed for comparison[13]. Another high incidence of 9% was reported from Japan very soon[12]. As time progressed, XGC continued to make its presence felt in numerous Indian studies with notable geographical variability (eg, Northern *versus* Southern India) quite analogous to the comparable variation in incidence of GBC. Krishnani *et al* in their Indian series of XGC, found a staggering coexistence of carcinoma gallbladder with XGC (19.6% of cases)[14]. A carcinomatous growth can obstruct the cystic duct raising the intra-GB pressure and can trigger the same thing what stones do in other cases. Moreover, malignant process causing breach in mucosa may further facilitate the growing inflammation in the stroma and further sequela[14]. However we did not find any such association in our small series.

The most frequent clinical presentation of patients in the pooled cohort was non-specific abdominal pain followed by other symptoms and signs typical of cholecystitis demonstrating that XGC is typically indistinguishable from cholecystitis on clinical assessment[5,7]. Gall stone is of course the strongest association but not present in every patient, indicating a role for additional aetiological factors[9]. Expectedly, those cases never demanded something extra ordinary unless presentation of Jaundice or lump distorted the picture. In our small series, not a single case has compelled us to think of advising any superior imaging like CECT other than routine sonology just on the basis of clinical grounds except in Case 1. Deep Jaundice in a 50 year old person at presentation and its sharp progression in Case 1 alerted us of malignant aetiology unless proved otherwise prospectively.

USG has its own limitations but surely can guide clinician towards need for further superior imaging, ie, CT scan, MRCP or EUS. Unsuspected thickening of GB wall, presence of mass or polyp in USG can open up the whole conundrum of differential diagnosis like Mirizzi syndrome or GB ca but prediction of XGC hardly arose in the horizon. In case module 1, 3, 4 & 5, unusual thickening of GB wall demanded CECT as next line of imaging.

No doubt, triphasic CT scan is still considered to be the best option around for dispelling the confusion and in making an pre-operative suggestion of XGC. Emphasis is usually made on wall thickening (focal or diffuse), Luminal Surface Enhancement (LSE), presence of intramural hypoattenuating nodules in thickened walls etc[15]. In XGC, Gall Bladder wall thickening can range from 4.0 mm to 18.5 mm and is usually diffuse in nature as observed in 88.9% and 87.8% of patients by two independent researchers Goshima *et al* and Zhao *et al* respectively[16,17]. Focal thickening is less commonly seen in XGC and is more likely to be associated with carcinoma of Gall Bladder[15]. The intramural nodules detected on imaging studies (85.7% and 61.1% by Zhao *et al* and Goshima *et al* respectively) usually represent either xanthogranulomas or abscesses[15-17]. Occupation of a large area of the thickened Gall Bladder wall by intramural nodules is highly suggestive of XGC[6].

XGC is pathology of gallbladder wall where mucosal surface mostly remains intact or hardly focally denuded[15]. On the contrary, carcinoma of Gall Bladder arises from the gallbladder epithelium and causes mucosal disruption in majority of the cases. Mucosal line disruption has been observed in 82.2% cases of carcinoma of Gall Bladderr. A continuous mucosal lining is more often observed with XGC (66.7% of cases) compared to a disrupted mucosal lining (33.3%)[17]. Luminal Surface Epithelium(LSE),defined as enhancement of the Gall Bladder wall predominantly at the luminal surface, was noted in 85.7% of cases by Zhao *et al* and 70% cases by Shuto *et al*[16,18].

Goshima *et al* set out five CT findings (eg diffuse Gall Bladder wall thickening, continuous mucosal lining, intramural hypoattenuating nodules in the thickened walls, absence of macroscopic hepatic invasion and absence of intrahepatic bile duct dilatation) to segregate XGC from carcinoma of Gall Bladder and interestingly found that diagnostic accuracy of XGC increases with the presence of three or more of the above mentioned findings[17].

Next comes the nature and extent of lymph nodal involvement where the observations of different researchers were varied. While Zhao *et al* have described an incidence of 10.2%, Goshima et alfound an incidence of 90%[16,17]. However, presence of regional lymphadenopathy is more prevalent in carcinoma compared to XGC[16]. While 58.9% cases with Gall Bladderr carcinoma had retroperitoneal lymph nodes enlargement, only 10.2% cases of XGC had mild lymph node enlargement (1-1.5 cm in diameter)[16]. In our series, case module 3,4 and 5 showed significant lymphadenopathy at porta but eventual diagnosis was XGC. Finally, CT findings like mass replacing Gall Bladder, intra-luminal mass or polypoidal mass-like thickening were yet to be seen in XC of different studies and same was the case in our series.

Despite those above mentioned distinctive CT features, the preoperative diagnosis remains ambiguous at its best which continues to be so or rather often gets further compounded in operation

invariably resulting iatrogenic injuries or surgical excess.

Now, decision of going forward with laparoscopic method when the possibility of XGC is there, is a matter of debate[19,20]. The intense chronic inflammation in XGC surely make the procedure hazardous and risky demanding painstaking dissection and good tissue respect. Multiple series of XGC has supported the safety of laparoscopy, but there is definitely higher incidence of conversion or iatrogenic injuries[5,20,21]. For us, as there is no luxury of suspecting XGC beforehand, the question of choosing laparoscopy or avoiding it never arose. Rather we went ahead with open method right from the beginning either in anticipation of sinister diagnosis (Case 1&4) or ambiguous pathology (Case 5). However, it is always better to adopt a low threshold for conversion, which enables a better assessment of the lesion and ensures superior outcomes with regard to mortality and morbidity[5,7,19,20].

In our series, the reasons behind the conversion from laparoscopy to open method are either lack of free access to abdomen via umbilicus or difficult anatomy (Case 2,5) or some iatrogenic injury (Case 2) prompted it. In Case 2, the stigma of past documented acute attack of cholecystitis is the likely explanation while in other cases of conversion and further misadventures, undocumented or missed history of acute cholecystitis or pancreatitis was readily blamed because of its potential to result inseparable adhesion. Whatsoever, the thought of XGC never tickled our imagination.

Operative findings in all our cases were varied, quite comparable with multiplex complications of XGC found in other studies, namely perforation, abscess formation, fistulous connection to duodenum or skin, and extension of the inflammatory process to the liver, colon, or surrounding soft tissues[22]. They all contribute to the confusing picture either resembling cases of calculous cholecystitis complicated with repeated attack or acute pancreatitis or simulating that of CA GB. Almost all our cases had gross inflammatory process,some limited to Gall Bladder only while few invading to surrounding viscera often culminating into fistulous connection like duodenum (Case 2), colon (Case 5). Often, it was a conglomerated mass of GB with surrounding viscera (Case 1,3 & 5). Or thanks to wall thickening and local destructive spread of inflammation or a conglomerated mass as in Case 1,3,4 & 5 it appeared as an advanced Gall Bladder carcinoma. Interestingly, it is also reported that both XGC and GBC may coexist, but latter may be masked by the masquerading features of the former[21].

In this scenario of overlapping features and the resultant ambiguity, the frozen section is expected to bring some clarity and help us fix the surgical strategy and avoid those unwanted exercise. Our experience was mixed as in Case module 1, frozen section helped us avoid unwanted excess surgery while in Case 3 & 5, the frozen section failed to comment conclusively hence forcing overzealous surgery for intention of oncological adequacy.

Now if we look back and judge all our cases in comparison with other databases from different studies, some interesting observations came up. Not a single case presented with clinically palpable lump. Jaundice never distorted the clinical picture except Case 1. Except Case 2,not a single case had documentable H/O acute attack of neither cholecystitis nor pancreatitis. So it can be said, unexplained gross and dense inflammatory process, which is typical of XGC ,is mostly a pathological phenomenon but clinically silent. In other way round, any operative field showing considerable adhesions and further sequelae in the absence of explainable past (eg, prior attack of cholecystitis or pancreatitis) should always raise the suspicion of XGC. Secondly, when a conversion (Laparoscopic to open Cholecystectomy) is followed by unplanned multivisceral surgery taking prolonged operating time, XGC must come in the differential diagnoses[21]. We also noted generally longer hospital stay than the usual.

Last but not the least, although XGC is a variant or aberration of Cholecystitis, it's more a radiologically (and of course Histopathologically) appreciable phenomena. Naturally, a senior radiologist has a portend role to play in minimising the misdiagnosis and associated hazards by putting particular stress on certain CT findings like the thickness of the Gall Bladder wall, patterns of wall thickening (focal versus diffuse), continuity of mucosal line (continuous versus disrupted), enhancement characteristics of mucosa (homogeneous versus heterogeneous), presence of submucosal hypo-attenuated nodules or bands and presence or absence of enlarged lymph nodes[8,15].

Talking of other advanced imaging in identifying XGC, Endoscopic Ultrasound (EUS) has shown remarkable accuracy of 93% in segregating GB Ca in a study of patients with suspected XGC and/or GB Ca[23]. But a negative sample cannot be conclusive. Secondly, sampling errors in EUS-FNA is another deterrent factor which limits its widespread applicability in XGC[21,23]. Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) also may be effective in diagnosing GB Ca,however, but it should

be interpreted with caution as XGC because of its inflammatory nature may yield a false-positive result[24,25].

So as the above mentioned CT findings are yet to considered conclusive in larger scale and EUS or PET scan still searching for encouraging note, intra-operative frozen section analysis is still considered our best bet in diagnosing XGC. So its liberal use will surely rule out simultaneous occurrence of GBC/XGC, thereby guiding optimum surgery and minimise unnecessary surgery in XGC patients[1,7,8].

Conclusion

Because of few confounding factors, eg, its allegiance to chronic Cholecystitis and GBC, otherwise two extremes of a spectrum, XGC will continue to be an puzzle for surgeons and surgical misadventures is unavoidable. Case series like ours, however small, will have some significant role to play in forcing certain issues. An increased awareness from the part of radiologist with focus on certain features combined with high degree of suspicion of surgeon combined liberal application of intra operative Frozen section can contribute to an algorithmic approach to XGC, thus ensuring appropriateness both to diagnosis and surgery.

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Original Article

Echocardiographic Evaluation of Diastolic Dysfunction in Patients with Type-2 Diabetes Mellitus in a Tertiary Care Centre of North Bengal

Bapilal Bala[1], Biswadev Basu Majumdar[2], Debanjan Roy[3], Jyotirmoy Pal[4], Achintya Narayan Ray[5], Debasis Chakrabarti[6] , Sekhar Chakraborty[7]

Aim : India shelters the most number of people with Diabetes Mellitus Worldwide. Diabetic Cardiomyopathy has a complex etiopathological causation and manifests commonly as Diastolic Heart Failure (DHF). Keeping the above result in consideration, the present research was done following proper scientific guidelines to determine the proportion of Ventricular Diastolic Dysfunction among Type-2 DM patients and to find an association between LV Diastolic Dysfunction and other indices such as age, HbA1c, DM duration and obesity.

Methods : In an observational case control study 172 subjects were evaluated for One year. The information obtained become analyzed using specific statistical techniques consisting of general deviation, mean, percent, multivariate evaluation, Z test, student 't'-test, and Chi square test, by the usage of SPSS-20 software program (Statistical package for the Social Sciences) for windows (SPSS, Chicago, IL). Some statistical exams like Chi-square tests and 't'-test has been achieved to have a look at qualitative and quantitative statistics with 'P' value <0.05 changed into measured statistically sizable.

Results : In our study out of 172 study subjects, majority (35.5%) belonged to 50-54 years age group and mean age of the study subjects was 49.02 (SD±7.628) years. The proportion of male population was higher (65.1%). Among the study subjects majority (46.5%) were overweight with Body Mass Index (BMI) between 25-29.9 kg/m2. In our study 12.2% study subjects had Fasting Blood Sugar (FBS) level more than 126 mg/dl and only 7.6% subjects had HbA1c level ≥7.5%. The proportion of Diastolic Dysfunction (DD) was much higher among the diabetic persons (60.46%) than the non diabetics (12.79%). Most of the study subjects had Grade I DD (61.9%) followed by Grade II DD (30.2%) and least having Grade III and IV DD. DD was much higher among persons having increasing Age,BMI, FBS and HbA1c level.

Conclusion : In this study we conclude that there has been a very significant connection of LV diastolic dysfunction with HbA1c levels, duration of Diabetes, Retinopathy, BMI, hypertriglyceridemia and autonomic neuropathy, as obtained by multivariate analysis. Earlier diagnosis and institution of treatment for DD will effect in better decline of the morbidity and Diastolic HF improvement.

[*J Indian Med Assoc* 2021; **119(10):** 36-41]

Key words **: Type 2 Diabetes, Diastolic Dysfunction.**

Type-2 Diabetes is the commonest type of Diabetes constituting 90% of the diabetic population in any country. The global prevalence of Diabetes is estimated to increase, from 4% in 1995 to 5.4% by year 2025[1]. A National Study of Diabetes Mellitus conducted in six major cities in India in 2000 showed that the prevalence of Diabetes among Urban adults was 12.1%. Prevalence of Impaired Glucose Tolerance (IGT) was also high (14.0%)[2]. Prevalence of diabetes was found to be lower in the low Socio-economic group living in urban areas compared with the high income group (12.6% *versus* 24.6% in subjects >40 years)[3]. The World Health Organization has predicted that the major burden will occur in the developing countries. There

Editor's Comment :

- The proportion of Diastolic Dysfunction was much higher among the Diabetic persons than the non diabetics.
- Most of the study subjects had Grade I DD followed by Grade II DD.
- DD increases with increment of ages of the study subjects, highest dysfunction was observed between ages 55-59 years.
- DD was much higher among persons having increasing BMI, FBS and HbA1c level and increase in duration of diabetes.

[1]MD (General Medicine), Associate Professor, Department of Medicine, Maharaja Jitendra Narayan Medical College and Hospital, Cooch Behar 736101

[2]MD(Medicine), DM(Cardiology), Senior Resident, Department of Cardiology, North Bengal Medical College and Hospital, Sushrutnagar 734012 and Corresponding Author

[3]MD (General Medicine), Consultant Physician, General Medicine, Desun Hospital, Siliguri 734012

[4]MD (General Medicine), Professor, Department of Medicine, RG Kar Medical College, Kolkata 700004

[5]MD (General Medicine), Associate Professor, Department of Medicine, Cooch Behar Government Medical College and Hospital, Cooch Behar 736101

[6]MD (General Medicine) Associate Professor, Department of Medicine, North Bengal Medical College and Hospital, Sushrutnagar 734012

[7]MD (Medicine), Consultant Physician and Diabetologist, Medical Director of Kins Care and Research Foundation and Kins Hospital, Siliguri 734005

Received on : 27/08/2020
Accepted on : 04/10/2021

will be a 42% increase from 51 to 72 million in the developed countries and 170% increase from 84 to 228 million, in the developing countries[5].

The only published nationally representative study on burden of DM in India is Prevalence of Diabetes in India Study – PODIS (2002), a multi-centric study (49 Urban and 59 Rural centers) on 41,000 Indian people. PODIS has estimated the age and gender standardized prevalence of DM in India to be 3.3 percent[6]. The International Diabetes Federation (IDF) also reported that the total number of diabetic subjects in India is 41 million in 2006 and that this would rise to 70 million by the year 2025[7]. Diastolic Heart Failure (HF) failure is the most common form of HF in DM with preserved ventricular systolic function. Studies have suggested an important increase in pre-clinical dysfunction among subjects with DM[8]. The purpose of this research would be to identify the amount of Diastolic Dysfunction in diabetes studies and its relationship to age, obesity symptoms, glycosylated Hb level and DM.

Materials and Methods

This study was conducted at the Cardiology Department of North Bengal Medical College for patients attending indoor and outdoor of Department of General Medicine for 1 year (July 2014- June 2015) . The age and sex matched controls will be selected from the persons who will accompany the patient.

Study Design : It is a observational case control study.

Inclusion Criteria :

All Type-2 DM subjects who are suffering from DM more than 5 years with normal left ventricular systolic function (LVEF:0.50%) having systolic blood pressure(SBP)<140 mmHg and diastolic blood pressure <90 mmHg not taking any anti-hypertensive medication.

Exclusion Criteria :

(a) All patients with indication of Coronary Artery Disease excluded by h/o angina and by ECG.

(b) All patients with indication of valvular Heart Disease.

(c) Hypertensive patients.

(d) Subjects with age > 60 years.

(e) Patients who will not provide consent for participation in the research study.

A similar type of study was done in Surat[9] which showed that among all cases of type-2 DM 66% had diastolic dysfunction.

Based on this, assuming P=66%, confidence interval= 95% and absolute precision of 10% sample size becomes:

Anticipated proportion of the population -P =66%

Confidence level -100(1-α) % =95%

Absolute correctness required on either side of proportion (in % points) -d =10%

Sample Size : $n = Z^2 1 - \alpha/2P(1-P)$

$d^2 = (1.96)^2 \times 0.66 \times 0.34$ $(0.1)^2$

= 86

Similar number of controls will be taken in 1:1 ratio. So, final sample size will be = 86+86 = 172.

Parameters to be Studied :

- History taking including duration from initial diagnosis of DM.
- General clinical examination:
- Anthropometric evaluation.
- Lipid profile

Echocardiographic Parameters :

(1) Peak E velocity in m/sec - peak early transmitral filling velocity during early diastole (normal: 0.5-0.8).

(2) Peak A velocity in m/sec – peak transmitral atrial filling velocity through late diastole (normal: 0.3-0.5).

(3) Deceleration Time (DT) in msec – time intervened among point where extrapolation of slowing slope of E velocity and peak E velocity crosses the zero baseline (normal:150-220).

(4) Isovolumetric Relaxation Time (IVRT) in msec – duration among mitral valve opening and aortic valve closure (normal: 60-100).

(5) Ratio of Peak E to peak A (E/A) (normal:1-2)

(6) E/e' ratio = mitral peak velocity of initial filling (E) to primary diastolic mitral annular speed (e') ratio (normal : >15)

Study Tools :

- Pre-designed and pre-tested interview schedule was used,
- The Consent Form is duly signed by the participant
- Sphygmomanometer,
- 2D, pulse wave Doppler and Tissue Doppler echocardiography.
- Electronic weighing machine,
- Measuring tape,

Study Techniques :

All patients who meet the informed consent procedure will be included in the study and data will be collected from a detailed history using a pre-test procedure; a complete clinical examination including routine tests, systemic tests and anthropometric tests will be performed. This will be followed by biochemical investigation using full Autoanalyser Machine (Transasia Biomedicals Limited ModeL XL-600). After twelve hours of fasting, the sample of blood has been collected and despatched to the laboratory of Biochemistry for added evaluation of the subsequent parameters:

- Plasma glucose level;
- GlycatedHbA1c;

- Lipid profile by crest biosystems reagent.

ECG will be done in all subjects.

Diagnostic Criteria :

Dyslipidemia: defined if TC >200 mg/dL; LDL cholesterol >130 mg/dL; HDL cholesterol 40 mg/dL: and TG >150 mg/dL.

Obesity indices: cut-off for high BMI >25 for female and>27 for males. Cut-off for excess Waist to Hip Ratio (WHR) > 0.9 for males and >0.8 for females. Cut-off for excess WC >80 cm for females and >90 cm for males.

Diabetes mellitus (DM): If a person is a identified diabetic on diabetes treatment or having FBS ≥126 mg/dL.

Diastolic dysfunction: LV diastolic dysfunction should be considered if any of the following is present.

- E/A ratio <1 or >2
- DT <150 or >220 ms
- IVRT <60 or >100 ms, or
- E/e' ratio >15

Statistical Methods : Data were collected, assembled and transferred to Excel Spread sheet (MS Excel 2007) and analyzed using IBM-SPSS 20 Chicago, IL .The t test and Chi Square Tests were used. All the statistical significance tests were done assuming Level of Significance at 95% confidence intervals.

Analysis and Results

Section 1: Background characteristics of the study subjects

Table 1 shows that, among 172 study subjects majority (35.5%) belonged to 50-54 years age group, followed by 31.5% in 55-59 years. Mean age was 49.02 (SD ±7.628) years of the study subjects.

Mean age of the study subjects was 49.02 (SD ±7.628) years. Majority of the population were males.

Among 172 study subjects majority (46.5%) of the study subjects had BMI between 25-29.9 kg/m² (overweight), 44.2% were of normal BMI. Whereas, obese were 2.9% and undernourished were 6.4%. Table 2 depicts that among all study subjects 12.2% had their fasting blood sugar level more than 126 mg/dl during the time of examination. This table shows that only 7.6% had their HbA1c level 7.5 or more than that.

Table 1 — *Distribution of the study subjects according to age group*

Age Group (years)	Frequency	Percent
40-44	19	11.0
45-49	38	22.0
50-54	61	35.5
55-59	54	31.5
Total	172	100.0

Section 2 : Characteristics of the Diabetic and Non-diabetic subjects.

Table 3 shows that though there is statistically significant difference with some important laboratory indices and BMI but there is no such difference in respect to age (Fig 1).

Table 4 shows there is statistically significant difference in Lipid Profile between Diabetic and Non diabetic subjects (p=0.000).

Section 3 : Diastolic dysfunction: proportion, grade and some important associated factors.

Table 5 shows that among all study subjects, 36.6% had Diastolic Dysfunction.

Table 6 shows that proportion of Diastolic Dysfunction was much higher among the diabetic patients (60.46%) than Non-diabetic persons (12.79%).

It is seen from Table 7 that Diastolic Dysfunction was found most using IVRT parameter.

Table 8 depicts that most of the subjects had Grade I Diastolic Dysfunction (61.9%), followed by Grade II DD among 30.2% and least having Grade III and IV DD.

Table 9 shows that proportion of DD increases with the increment in age of the subjects. Highest Dysfunction was observed among subjects having age of 55 to 59 years (31.5%). This finding is statistically non-significant.

This Table 10 shows that proportion of DD was much higher (60.9%) among the subjects having HbA1c level

Table 2 — *Baseline Characteristics of the population*

Age (Mean ± SD)	49.02 (SD±7.628) years		
Gender (M: F= 1.86)	Male : 112 (65.1%)		Female : 60 (34.9%)
BMI	<18.5 ; 11(6.4%)	18.5-24.9 ; 76(44.2%)	25-29.9 ; 80 (46.5 %) ≥30 ; 5 (2.9 %)
Fasting Blood Sugar (FBS)	<100 mg/dl ; 97(56.4 %)	100-125 mg/dl ; 54(31.4 %)	≥126 mg/dl ; 21 (12.2 %)
HbA1c	<6.5 ; 124(72.1 %)	6.5 – 7.4 ; 35(20.3 %)	≥7.5 ; 13 (7.6 %)

Table 3 — *Association of some important parameters between diabetic and non-diabetic patients* (n=172)

Parameters	Diabetic (mean ± SD)	Non-diabetic (mean ± SD)	Statistical test (95% CI, t-test, p value)
AGE	49.01 ± 7.438	49.02 ± 7.856	- 2.315 to 2.291, t value = -0.010, p= 0.992
BMI	26.41 ± 1.886	21.12 ± 2.305	4.654 to 5.922, t value = 16.466, p= 0.000
FBS	110.16 ± 21.101	91.56 ± 13.882	13.228 to 23.98, t value = 6.831, p= 0.000
PPBS	185.53 ± 50.419	121.45 ± 10.861	53.103 to 75.060, t value = 11.521, p= 0.000
HBA1C	6.53 ± 0.846	5.14 ± 0.434	1.184 to 1.589, t value = 13.519, p= 0.000

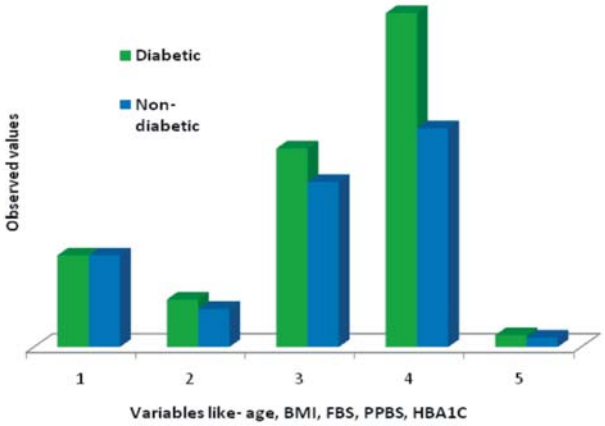

Fig 1 — *Mean values of some baseline parameters between diabetic and non-diabetic patients*

more than 7. The above result is statistically significant ($p<0.05$).

Table 11 shows that proportion of DD increases with the increase in duration of diabetes of the subjects. This finding is statistically significant ($p<0.05$).

From the Table 12 it is seen that, diastolic dysfunction is much higher among the subjects who had increased BMI, Fasting blood sugar and HbA1c.

Table 13 shows that occurrence of diastolic dysfunction is suggestively associated with many of the echo parameters, except the IVRT value.

Discussion

Our result reveal that Asymptomatic Cardiac Dysfunction is common in subjects with DM. It has been widely described as DiastoliC Dysfunction in subjects with normal Systolic function, and there are not any signs and symptoms of heart failure (HF). It reveals that fasting BSL, HbA1c, serum TC, serum TG and LDL cholesterol in case the values are higher versus the control group. A total of 52 subjects (60.46%) among the trial group had diastolic dysfunction, on the other hand 11 (12.79%) within the control group showed Diastolic Dysfunction. The duration of diabetes mellitus of ≥15 years was significantly higher than Diastolic Dysfunction ($P<0.05$). Patients having HbA1c more than 7.0% had a surge in Diastolic Dysfunction than patients with HbA1c less than 7.0% ($P<0.05$). Diastolic dysfunction was proportionally high in subjects with more than 55-year age compared to less than 55-year age subjects.

We have compared our study findings with many studies. Soldatos *et al*[10]. In their study of 55 control subjects with type 2 DM it has been found that diastolic dysfunction has been present in a big proportion of patients with Type-2 DM. Equally, in our study, 60.46% of patients among the study group had Diastolic Dysfunction and 11 (12.79%) among the control group had Diastolic Dysfunction ($P<0.05$). Diabetes is thought to increase strength through myocardial collagen placement and high-end glycation end products.

In the case control study of 77 normotensive

Table 4 — *Association of some important parameters related to Lipid Profile between diabetic and Non-diabetic patients (n=172)*

Parameters	Diabetic (mean ± SD)	Non-diabetic (mean ± SD)	Statistical test (95% CI, t-test, p value)
LDL	130.48 ± 19.986	118.05 ± 8.435	7.812 to 17.048, t value= 5.314, p= 0.000
TC	208.12 ± 22.037	176.08 ± 12.711	26.62 to 37.45, t value =11.678, p= 0.000
HDL	40.60 ± 4.625	48.85 ± 5.416	-9.76 to -6.728, t value= -10.735, p= 0.000
TG	151.07 ± 15.756	133.72 ± 10.435	13.32 to 21.37, t value= 8.513, p= 0.000

Table 5 — *Proportion of Left Ventricular Diastolic Dysfunction among patients and controls (n=172)*

Diastolic dysfunction	Frequency	Percentage
Present	63	36.6
Absent	109	63.4
Total	172	100

**Assessed using all echo parameters*

Table 6 — *Distribution of Diastolic Dysfunction among Diabetic and Non-diabetic Study Subjects (n=172)*

Diabetes Mellitus	Diastolic dysfunction		Total
	Present	Absent	
Yes	52 (60.46)	34 (39.54)	86 (100)
No	11 (12.79)	75 (87.21)	86 (100)
Total	63 (36.6)	109 (63.4)	172

Z test value = 6.33, 95% CI value= 33.99 to 61.35
P value = 0.000

Table 7 — *Diastolic dysfunction according to various Echo parameters (n=172)*

Echo parameters	Frequency	Percent
E/A	44	25.6
IVRT	85	49.5
DT	68	39.5
E/e'M	26	15.1
E/e'L	8	4.7

Table 8 — *Pattern of Left Ventricular Diastolic Dysfunction among Patients and Controls* (n=63)

Grades of diastolic dysfunction	Frequency	Percentage
Grade I	39	61.9
Grade II	19	30.2
Grade III and IV	5	7.9
Total	63	100

Table 9 — *Relationship of Diastolic Dysfunction with age group (n=172)*

Age group (years)	Diastolic dysfunction		Total
	Present	Absent	
40-44	4 (21.1%)	15 (78.9%)	19 (100.0%)
45-49	10 (26.3%)	28 (73.7%)	38 (100.0%)
50-54	13 (21.3%)	48 (78.7%)	61 (100.0%)
55-59	17 (31.5%)	37 (68.5%)	54 (100.0%)
Total	44 (25.6%)	128 (74.4%)	172 (100.0%)

Chi-square value= 1.787, p value= 0.618

Table 10 — *Relationship of Diastolic dYSFUNCTION WITH HBA1C (N=86)*

HbA1c	Diastolic dysfunction		Total
	Present	Absent	
< 7	20 (31.7%)	43 (68.3%)	63 (100.0%)
≥7	14 (60.9%)	9 (39.1%)	23 (100.0%)
Total	34 (39.5%)	52 (60.5%)	86 (100.0%)

Chi-square value= 5.987, p value= 0.014

Table 11 — *Relationship of Diastolic Dysfunction with Duration of diabetes (n=86)*

Duration of diabetes (years)	Diastolic dysfunction		Total
	Present	Absent	
5 - 9	17 (29.8%)	40 (70.2%)	57 (100.0%)
10 -14	14 (56.0%)	11 (40.0%)	25 (100.0%)
≥15	3 (75.0%)	1 (25.0%)	4 (100.0%)
Total	34 (39.5%)	52 (60.5%)	86 (100.0%)

Chi-square value= 7.188, p value= 0.027

Table 12 — *Association of left ventricular diastolic dysfunction with some baseline parameters (n=172)*

Baseline Parameters	Diastolic dysfunction (mean ± SD)		Statistical test (95% CI, t-test, p value)
	Present	Absent	
BMI	26.15 ± 2.68	22.94 ± 3.21	-2.134 to 4.265, t value = 5.929, p= 0.000
FBS	108.3 ± 21.97	98.3 ± 18.84	3.202 to 16.780, t value = 2.905, p= 0.004
HbA1c	6.46 ± 1.08	5.62 ± 0.82	0.531 to 1.150, t value = 5.369, p= 0.000

Table 13 — *Correlation of some important parameters related to echocardiography findings between patients having diastolic dysfunction or not (n=172)*

Echo Parameters	Diastolic dysfunction (mean ± SD)		Statistical test (95% CI, t-test, p value)
	Present	Absent	
IVRT	77.82 ± 32.178	72.35 ± 20.173	-2.740 to 13.673, t value = 1.315, p= 0.190
DT	225.30 ± 48.760	199.84 ± 34.313	12.176 to 38.727, t value = 3.785, p= 0.000
E/e'M	13.67 ± 5.39	9.73 ± 2.78	2.687 to 5.190, t value = 6.212, p= 0.000
E/e'L	11.44 ± 4.41	8.91 ± 2.33	1.496 to 3.564, t value = 4.832, p= 0.000
E/A	0.99 ± 0.56	1.27 ± 0. 17	-0.398 to -0.177, t value = -5.156, p= 0.000

patients Masugata ET AL observed that diastolic dysfunction without LV systolic dysfunction in subjects with accurately controlled Type-2 DM was not linked to high blood pressure or LV hypertrophy, but rather type 2 DM and aging. Likewise, in the current study, a 60.46% of patients from the study group without hypertension and CAD had diastolic dysfunction with normal LV systolic function.Ordinary LV systolic and diastolic activity are related with the period of diabetes and other diabetic microangiopathies, like diabetic retinopathy and neuropathy.

These findings are similar to the current study findings, wherein diastolic dysfunction exist in several patients in long-standing researches. The diabetic length more than 15 years had a greater frequency of diastolic dysfunction linked to the 5 - 9 year group (P<0.05).

In case-control study of 71 patients with type-2 DM, Mishra *et al*[11] found that patients with type 2 diabetes had lesser LV systolic and Diastolic function associated with fit patients. Likewise, in the present study, duration of diabetes more than 15 years had advanced occurrence of diastolic dysfunction compared to the 5–9-year-old age group (P<0.05).

In the study of 114 subjects Exiara *et al*[13] found that the prevalence of LV diastolic dysfunction in subjects with normotensive, asymptomatic and well-controlled DM Type-2 is higher, and rises with age. Almost 63.2% of subjects previously had diastolic dysfunction in their research paralleled 60.46% study subjects in the present study. In the study conducted by Diamant *et al*[14] reveal that early (E) acceleration rate, deceleration peak, high fill rate and E / A ratio, and also many other indicators of diastolic activity, are suggestively lesser in subjects with type 2 diabetes. 2 newly discovered, well-controlled and relatively simple controls (P<0.02). The above results are similar with our findings.

Study conducted by Bonito, *et al*[15] found that impaired LV diastolic dysfunction happens initially in the natural history of Type 2 DM and is associated to clinical proof of microangiopathic conditions. In the study conducted by Aaron *et al*[16] reveal that among the 1,760 patients with diabetic, 411 (23%) patients had diastolic dysfunction which is having high prevalence of adverse outcomes in important number associated to those short of diastolic dysfunction.

The above results are similar with our findings.

In the study conducted by Boyer *et al*[17] reveal that the rate of LV diastolic dysfunction in normotensive subjects without signs with Type 2 Diabetes is higher. Diastolic Dysfunction was present in 75% subjects. In the study conducted with 305 patients with type-2 DM by Poulsen *et al*[18] reveal that, irregular filling of LV was highly linked with abnormal myocardial perfusion scintigraphy.

In the study of 544 consecutive Japanese DM subjects with ejection fraction ≥50%, Takeda *et al*[19] reveal that Diastolic Dysfunction played a major role in HF symptoms with average systolic function in DM subjects, regardless of the blood sugar status or renal dysfunction. Above findings are somewhat comparable to the present study in which diastolic dysfunction was suggestively higher at HbA1c more than 7.0%.

Hameedullah *et al*[20] in their study of 60 patients with Type-2 DM they found a strong association

between HbA1c level and Diastolic indicators (P<0.05). Diastolic dysfunction was further common in highly managed diabetic patients and its sternness was linked with glycemic control. Likewise in the present study, HbA1c>7.0% had a high rate of diastolic dysfunction compared to HbA1c <7.0%.

In the study of 87 patients, CM Schannwell *et al*[21] revealed that even younger patients with Diabetes suffer from diastolic dysfunction, while systolic ventricular function is standard. Accordingly, we say that patients with Type-2 DM is highly linked with duration of Diabetes, HbA1c, age, dyslipidemia and variability in different indicators of obesity.

Our study reveals that cases of pre-clinical diastolic dysfunction are extremely high in patients with Type 2 DM. Our study also reveal that there is a straight link between duration of Diabetes and Diastolic Dysfunction; also, that statistically significant diastolic dysfunction occurs more than five years after the beginning of diabetes irrespective of co-existent coronary artery disease or hypertension. Accordingly, more studies have to be conducted to prove the hypothesis that screening and treatment of subjects with pre-clinical DM can postpone the development of Heart Failure.

Limitations :

(1) The study was conducted on general population in India. Therefore, the results found in our study need further research among different ethnic and racial group.

(2) The Homeostatic Model Assessment (HOMA) test model to investigate fasting insulin concentration has not been involved in our study due to limitations of resources. HOMA index is considered an independent component of Diastolic Dysfunction.

(3) There are both technical and clinical limitations. For technical limitations, proper attention to the location of the sample size, as well as gain, filter and minimal angulation with annular motion, is essential for reliable velocity measurements.

(4) With experience, these are highly reproducible with low variability. Because time interval measurements are performed from different Cardiac cycles, additional variability is introduced. This limits their application to selective clinical settings in which other Doppler Measurements are not reliable.

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Original Article

Early Enteral Feeding In Cases of Gastrointestinal Anastomosis and Perforation Sututring : A Prospective Study

Akshat Mishra[1], Girish D Bakhshi[2], Ajay H Bhandarwar[3]

Bowel Anastomosis and perforation suturing are among the commonest procedures performed by general surgeons worldwide in both elective and emergency settings. The traditional rule of thumb has been to keep these patients' nil by mouth in the postoperative period till the return of bowel sounds. The reasoning behind this practice was to protect the anastomotic site and provide the gut with rest till return of normal function. Recently, studies have shown that early enteral feeding not only hastens the return of bowel function but also significantly reduces the length of postoperative stay without causing any complications.

This prospective study was carried out on 100 patients undergoing resection and anastomosis and/or perforation suturing in either elective or emergency setting. Patients were randomly selected and divided into a study group and control group of 50 patients each. The patients in the study group received early enteral feeding, started within 8 hours postoperatively in the form of 50ml/hour. Patients in the control group were started on clear liquids once bowel sounds returned. Patients were then monitored for a multitude of postoperative conditions and complications while diet was gradually advanced in both groups.

From the study, it becomes apparent that patients receiving early enteral feeding showed a marginal improvement in postoperative nausea and vomiting. These patients reported significantly lower scores of postoperative pain on visual analogue scores and significant decrease in abdominal girth. The patients in the study group showed an early resolution from postoperative ileus as evidenced by earlier passage of flatus and stools. Their mobility was better with lesser days required to carry out daily tasks and attend the bathroom unassisted. The length of hospital stay was significantly shorter in the study group. Finally, the rate of postoperative complications were similar in both groups.

[*J Indian Med Assoc* 2021; **119(10):** 42-6]

Key words **: Gastrointestinal Anastomosis, Perforation Sututring.**

Bowel anastomosis and perforation suturing are commonly performed procedures by general surgeons worldwide. While primary repair of perforations is largely done as emergency procedures, resection and anastomosis is commonly done in emergencies primarily for obstructive causes and electively for oncological aetiologies[1].

The traditional practice after major gastrointestinal surgeries is to keep the patient nil by mouth to prevent postoperative nausea and vomiting and protect the anastomotic site till return of bowel function.Recently emphasis has been given to initiating early enteral feeding within 6 to 24 hours in the postoperative period. Early enteral feeding is believed to reduce stress response, improve immunological response and promotes wound healing while significantly reducing septic complications after major abdominal procedures[2]. This is chiefly due to enterocyte growth stimulation which results in an improved mucosal barrier function and decreased bacterial translocation[3].

Editor's Comment :

- Early enteral feeding reduces stress response and improve immunological response.
- Early enteral feeding after GI anastomoses and perforation suturing is safe and we'll tolerated.

The initiation of early enteral feeding hastens the return of bowel function and has an overall positive effect on the patients care by permitting early weaning form intravenous fluids and drugs, permits early mobility and significantly helps in reducing the postoperative length of hospital stay.

This study is an attempt to validate the methods for objectively assessing the effects of early enteral feeding initiated in patients undergoing bowel anastomosis and perforation suturing in both elective and emergency setting.

Materials and Methods

This is a prospective study conducted over a period of 30 months from June 2018 to March 2021 at a tertiary care centre. The objective of the study was to

Department of General Surgery, Grant Government Medical College and Sir JJ Group of Hospitals, Mumbai 400008

[1]MBBS, MS, Registrar and Corresponding Author

[2]MBBS, MS, DNB, MRCS, Ed UK, FACS, Professor and Unit Head

[3]MBBS, MS, FICS, FIAGES, FACS, Professor and Head

Received on : 26/03/2021

Accepted on : 05/10/2021

study the feasibility, safety and efficacy of early enteral feeding after gut anastomosis and/or perforation suturing and evaluation of tolerance of early enteral feeding, assessment of postoperative nausea, vomiting, postoperative ileus and complication and the length of hospital stay.

Inclusion criteria :

- All cases of patients undergoing exploratory laparotomy with resection anastomosis or perforation suturing in the gastrointestinal tract on an emergency or elective basis.
- Age group between 12 to 60 years males and non-pregnant females.
- Patients willingly giving consent

Exclusion criteria :

- Age of the patient below 12 years and above 60 years
- Pregnant women
- Patients not willing to participate in the study.

Sample size and distribution :

- 100 patients
- Patients were divided in a study group and a control group comprising of 50 patients each.
- Randomisation was done on an odd-even basis.

Study design :

- Patients in the study group were started on an early enteral feeding protocol 8 hours after surgery. They were started on 50ml/hr of water/clear liquids on postoperative day 1, 8 hours after surgery. Clear liquids were continued on postoperative day 2. On postoperative day 3, unclear liquids/milkshakes were administered followed by a soft diet on postoperative day 4 and a full diet on postoperative day 5.
- Patients in the control group were started on oral feeding with clear fluids after resumption of bowel sounds confirmed on auscultation. Once tolerated, they were gradually shifted based on vital parameters and general physical condition to unclear liquids, soft diet and full diet in order.
- The patients were subjected to a thorough clinical workup which included appropriate laboratory and radiological investigations both prior and post-surgery as required.
- On each of the 5 days postoperatively, the patients in both the groups were monitored for abdominal girth, nausea and vomiting, and pain as per visual analogue scale. The passage of flatus and stools, ability to visit the washroom unassisted and ability to carry out routine tasks unassisted were also observed. Finally, the length of stay of the patients in each group was compared.

Data analysis :

All the data collected from the patients was compiled in a Microsoft Office Excel Sheet and analysed. Results are shown in a Tabular and Graphical format. Appropriate Statistical test was applied whenever necessary.

Observations

Age and Sex Distribution :

Mean age for patients was 36.58 years in the study group and 39.34 in the control group. Majority of the participants in the study belonged to the 4th decade of life. After applying unpaired T test, the p value was 0.281, hence both groups were comparable with respect to age distribution.

In both the groups, there were 17 female patients and 33 male patients. After applying the unpaired T test, the P value for sex wise distribution was 1, hence both groups were comparable in terms of sex-based distribution.

Nature of Surgery :

In the study group, 38 patients were operated in the elective setting while 12 patients were taken up in the emergency setting. In the control group, 36 patients were taken up in the elective setting while 14 patients were operated in emergency setting. After applying the student T test, the P value was 0.648, hence both groups were comparable in terms of nature of surgery performed.

Indication for Surgery :

The most common indication for surgery in both the groups was for ostomy closure with 17 patients in the study group and 18 patients in the control group. In terms of ostomy closure, 9 patients in the study group and 11 patients in the control group were operated for ileostomy closures. The second most common surgery performed in the elective setting was resection and anastomosis for carcinoma colon with 9 patients in both groups operated for the same. The most common surgery done in the emergency setting for both groups was perforation suturing for prepyloric perforation (6 in study group and 6 in the control group) (Table 1).

Assessment of Postoperative Parameters :

Postoperative Nausea and Vomiting —

In the control group, 19 patients developed nausea on POD 1 and by POD 5, two patients still complained of postoperative nausea. In the study group, 10 patients complained of nausea on POD 1 and no patient reported postoperative nausea beyond POD 3. On applying unpaired T test, there was significant

Table 1 — *Comparison of demographic profile and baseline data of the study group and control group*

Parameter	Study Group	Control Group	P Value	Significance
Age (Mean) in years	36.58±12.477	39.34±12.98	0.281	Not significant
Sex (M/F)	33/17	33/17	1	Not significant
Nature for surgery :				
Elective	38	36	0.648	Not significant
Emergency	12	14		
Indication for Surgery :				
Bariatric Surgery	1	1	0.687	Not significant
Caecal perforation	1	1		
Carcinoma Colon	8	9		
Colostomy closure	4	5		
Enterocutaneous fistula	3	2		
Ileal Perforation	4	3		
Ileostomy closure	9	11		
Intussusception	2	0		
Jejunal perforation	1	2		
Prepyloric perforation	6	9		
Stricture	4	5		
Sigmoidostomy closure	4	2		
Carcinoma stomach	3	0		

reduction in postoperative nausea on POD 1,2 and 4.

In the control group, 7 patients reported at least 1 episode vomiting on POD 1. No patient reported any episode of vomiting beyond POD 3. In the study group, 3 patients reported vomiting on POD 1. There were no reported episodes of vomiting beyond POD 1. On applying the unpaired T test, there was significant difference only on POD2.

Visual Analogue Scale for Postoperative Pain :

The mean visual analogue score for postoperative pain on POD 1in control group was 6.08 and 5.16 in the study group. The mean scores from POD 2 to POD 5 were remarkably lower in the study group with the difference reaching statistical significance on applying the student T test.

Abdominal Girth —

The percentage decrease in abdominal girth in the next two postoperative days were 0.575% and 1.3% for the control group and 14.07% and 2.07% for the study group. On applying the student T test, there is significant difference between the two groups on all postoperative days.

Days Required to Visit the Bathroom Unassisted —

The earliest postoperative day for patients to visit the bathroom unassisted was POD 3 in the control group (16/50) and POD 1 in the study group (10/50). All patients were able to visit the bathroom unassisted by POD 7 in the control group and POD 4 in the study group. On applying the student T test, there is significant difference between the two groups with patients in the study group able to visit the bathroom unassisted at a significantly faster rate than patients in the control group.

Days Required to Carry Out Daily Tasks Unassisted —

The earliest postoperative day for patients to carry out daily tasks unassisted was POD 4 in the control group (4/50) and POD 2 in the study group (6/50). All patients were able to visit the bathroom unassisted by POD 9 in the control group and POD 6 in the study group. On applying the student T test, there is significant difference between the two groups with patients in the study group able to carry out daily tasks unassisted at a significantly faster rate than patients in the control group.

Passage of Flatus and Stools —

The earliest postoperative day when patients were able to pass flatus and stools in the control group was POD 3 (3/50) and POD4 (4/50) respectively. In the study group, the earliest patients were able to pass flatus and stools was by POD 2 (16/50) and POD 2 (1/50). All in all, all patients were able to pass flatus and stools by POD 7 and POD 8 in the control group and POD 4 and POD 7 in the study group respectively.

On applying student T test, there is significant difference in terms of passage of flatus and stools between the two groups, hence it can be inferred that early enteral feeding is associated with an earlier passage of flatus and stools and earlier resolution of postoperative ileus.

Postoperative Fever —

12 the control group and 10 patients in the study group reported fever between POD 1 and POD 5. On applying student T test, there is no significant statistical difference between the two groups.

Surgical Complications :

2 patients in the control group and 1 patient in the study group developed intraabdominal abscess that needed either percutaneous drainage or re-exploration. 8 patients in the control group and 5 patients in the study group developed superficial skin dehiscence. The difference between the two groups in terms of surgical complications does not reach statistical significance.

Length of Postoperative Hospital Stay :

The minimum postoperative stay was 7 days for the

control group and 5 days for the study group. The mean length of hospital stay was 12.36 days for the control group and 8.78 days for the study group with the difference reaching statistical significance on applying the student T test (Table 2).

Table 2 — *Comparison of postoperative parameters among the two groups*

Parameter	Study Group	Control Group	P Value	Significance
Postoperative Nausea :				
POD 1	10	19	0.047	Significant
POD 2	3	10	0.037	Significant
POD 3	2	4	0.24	Not Significant
POD 4	0	4	0.041	Significant
POD 5	0	2	0.153	Not significant
Postoperative Vomiting :				
POD 1	3	7	0.182	Not significant
POD 2	0	5	0.022	Significant
POD 3	0	2	0.153	Not Significant
POD 4	0	0	-	
POD 5	0	0	-	
Visual Analogue Scale for Postoperative Pain (Mean) :				
POD 1	5.16	6.0	<0.001	Significant
POD 2	4	5.24	<0.001	Significant
POD 3	3.42	4.28	<0.001	Significant
POD 4	2.8	3.34	<0.001	Significant
POD 5	2.12	2.64	<0.001	Significant
Abdominal Girth (In cm) :				
POD 1	75.26	80	0.036	Significant
POD 2	74.18	79.54	0.017	Significant
POD 3	73.7	78.96	0.019	Significant
Days Required to go to Bathroom Unassisted (Mean) :	2.1±0.7354	4.16±0.9971	<0.001	Significant
Days Required to Carry Out Daily Tasks Unassisted (Mean) :	3.74±0.9649	5.90±1.165	<0.001	Significant
Passage of Flatus (n) :				
POD ≤3	40	3	<0.001	Significant
POD > 3	10	47		
Passage of Stools (n) :				
POD ≤4	28	4	<0.001	Significant
POD > 4	22	46		
Postoperative Fever (n) :	10	12	0.629	Not significant
Surgical Complications (n) :	6	8	0.274	Not significant
Postoperative Stay In Days (Mean) :	8.78±6.431	12.36±4.881	0.002	Significant

Discussion

Traditionally, conventional feeding practices in the postoperative patient undergoingmajor gastrointestinal surgeries dictates keeping the patient nil per oral for a prolonged duration till the return of normal gut motility. The dictum believes that keeping the patient nil per oral would provide the gut with adequate rest which would aid in anastomotic site and wound healing.This practice is still regarded as safe and commonly practiced worldwide. Recently, this approach has been intensely questioned and multiple studies have shown no significant advantage in delaying postoperative feeding in patients undergoing major gastrointestinal surgery. In a meta-analysis conducted by Lewis et al [4], consisting of 13 trials, the key message was that there was no obvious benefit in keeping patients nil by mouth with early enteral feeding assisting in reducing septic complications and length of stay while improving wound healing.

In the present study, the two groups were statistically comparable in terms of age and sex distribution. Majority of the patients in both groups underwent surgery in the elective setting. The most common indication for surgery in both groups was for ostomy closure with majority being ileostomy closure. Resection of colonic malignancies were the second most common elective procedures while repair of prepyloric perforation was the most common procedure done in emergency. The groups were statistically comparable in terms of nature and indications for surgery.

In the present study, the study group were started on clear fluids orally or via a nasogastric tube 8 hours after surgery at 50ml/hour, with gradual progression to unclear fluids and milk shakes on postoperative day 3 and soft and full diet on postoperative day 4 and 5 respectively. In contrast, the control group was started on clear liquids only after resumption of bowel sounds postoperatively and gradually progressed based on clinical recovery to further diet advancements.

In the present study, the study group reveals significant difference from the study group in postoperative nausea only on the early postoperative days while no such distinction can be made between the two groups in terms of vomiting. However, there are no increased numbers of such cases in the study group. In a study conducted by Hartsell *et al*[5], the results are similar. Hence, it can be concluded that early enteral feeding is not associated with an increase in postoperative nausea and vomiting.

The two groups show significant difference in terms of postoperative pain and abdominal girth with the study

group showing markedly lower mean scores for postoperative pain during the first 5 postoperative days as well as a greater percentage decrease in abdominal girth. Hence, patients receiving early enteral feeding show a better recovery profile in comparison to patients on traditional delayed feeding.

In the present study, the mean number of days taken by patients in the study group to visit the bathroom unassisted is 2.1 days with a standard deviation of 0.7354, while that for the control group is 4.16 days with a standard deviation of 0.9971 with the difference reaching statistical significance. For the time taken to carry out daily tasks unassisted, the mean number of days taken by the patients in the study group is 3.74 days with a standard deviation of 0.9649 and for the control group is 5.90 days with a standard deviation of 1.165 with the difference reaching statistical significance. In terms of early mobilisation, patients in the early enteral feeding arm of the study show an earlier return to daily activity and a faster recovery time postoperatively. As early mobilisation and quicker recovery in the postoperative phase are key components of the ERAS protocol[6], this study is in tune with the current practices advocated all over the world.

Passage of flatus and stools is an age old but reliable indicator of resolution from postoperative ileus (POI). POI is defined as inhibition of propulsive bowel activity following surgery that usually manifests with obstipation, nausea, vomiting and abdominal distension. It has generally been accepted that despite the numerous advances in the field of medicine, POI is considered an acceptable outcome following gastrointestinal surgeries. For the patient, POI serves as a severe distress that is responsible for significantly delaying recovery and increasing the length of hospital stay. In the present study, more than 40 patients in the study group were able to pass first flatus on or before the 3rd postoperative day while only 3 patients were able to do so in the control group. Similarly, 28 patients in the study group and only 4 patients in the control group were able to pass their first stools on or before the 4th postoperative day with the difference reaching statistical significance. Hence, early enteral feeding is associated with the faster recovery from postoperative ileus as documented by a much early passage of flatus and stools than delayed conventional feeding. Similar findings were corroborated by a similar study conducted by Pragatheeswarane *et al*[7]. This could be attributed to stimulation of bowel peristalsis by early feeds.

In the present study, the incidence of postoperative fever and postoperative complications is similar in both groups. Tian *et al*[8], El Nakeeb *et al*[9] and Vaishnani *et al*[10] have all reviewed the same findings in their studies with no significant differences between the early enteral feeding and traditional group. The present study did not report any increased number of cases with the same and hence early feeding is not associated with an increased number of complications.

Majority of the studies reviewing the efficacy of early enteral feeding have kept the length of hospital stay as the primary outcome. In the present study, the mean duration of postoperative stay was 8.78 ± 6.431 days in the study group and 12.36 ± 4.881 days in the control group with the difference reaching a statistical significance. A shorter hospital stay provides an improved quality of life to the patient, is psychologically better and has cost benefit to the hospital.

In conclusion, early enteral feeding after gastrointestinal anastomosis and perforation suturing in both the elective and emergency setting is safe, well tolerated by the majority of patients and significantly reduced the length of postoperative ileus, length of postoperative stay and improves clinical outcomes. Thus, it should be considered the norm and not the exception in present day surgical practice.

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Review Article

Laparoscopy in the Era of COVID-19 Pandemic : Lessons Learned from PIPAC Surgery

Soumen Das[1], Biswarup Bose[2], Anurag Chaudhuri[3], Rishin Dutta[4], Kamalesh Rakshit[5], Anirban Nag[6]

COVID-19 pandemic has created a havoc healthcare problem. Day to day Surgeries specially Laparoscopic Surgeries being aerosol generating procedures are being avoided by majority of Surgeons. But it is time to adopt the 'new normal'. Pressurized Intra Peritoneal Aerosol Chemotherapy (PIPAC) is a technique where aerosol Chemotherapy is instilled into peritoneal cavity via an injector (CapnoPen). Leakage of chemotherapy into the atmosphere is prevented by some special techniques. Here we discuss the principles of PIPAC, which if applied in routine laparoscopic Surgeries, will reduce the chance of aerosol contamination and will the make the procedure safe.

[*J Indian Med Assoc* 2021; **119(10):** 47-9]

Key words **: COVID-19 pandemic, Laparoscopy, Minimally Invasive Surgery, PIPAC.**

The outbreak of Corona Virus (COVID-19) has brought about an unprecedented circumstance leading the entire World in a fight against the pandemic. Similarly, Surgical practice faces challenges in a balancing act between patient care and to minimize transmission among Health care workers. Laparoscopic surgery is no exception.

A genus of the *Coronaviridae* family, Corona virus is an enveloped virus with a large plus-strand RNA genome which is 27-32 kb in size, capped and polyadenylated[1]. Peiris *et al*[2] reported that Novel Corona Virus is the probable cause of Severe Acute Respiratory Syndrome (SARS).

Holmes KV[3] proposed that the SARS-associated Corona Virus could have emerged as a genetically modified form of a human Corona Virus that acquired new virulence factors or as a genetic modification of an animal Corona Virus with the capability of infecting human cells. According to the same author, consolidation of two human Corona Viruses or recombination of a single human corona virus and an animal Corona Virus is also a possibility[3].

Department of Surgical Oncology, Netaji Subhas Chandra Bose Cancer Hospital, Kolkata 700094

[1]MS, FACS, MRCS (Edinburgh), FRCS (Glasgow), Chief Consultant and Corresponding Author

[2]MS (Surgery), Associate Professor, Department of Surgery, ESI-PGIMSR & ESIC Medical College, Joka, Kolkata 700104

[3]MBBS, IPGME&R and SSKM Hospital, Kolkata 700020

[4]MS (Surgery), Resident, Department of Surgery, IPGME&R, SSKM Hospital, Kolkata 700020

[5]MS (Surgery), Associate Consultant

[6]DNB (Surgery), Associate Consultant

Received on : 30/03/2021

Accepted on : 14/04/2021

Editor's Comment :

- Laparoscopic surgery is associated with less pain, magnified vision, less blood loss, less hospital stay. But Laparoscopic Surgery during COVID-19 infection ponders higher risk of viral spread through aerosol. This aerosol spread can be prevented by the adoption of different techniques used during PIPAC surgery.

Mostly three human corona viruses have been studied in detail among which HCoV-229E and HCoV-OC43 were identified in the mid-1960s and are responsible for common cold[4-12]. Similarly, the third type SARS-CoV, the most pathogenic human Corona virus, has been found to cause a life-threatening pneumonia[13-15].

Federico Coccolini *et al*[16] demonstrated the presence of SARS-CoV-2 in peritoneal fluid in COVID-19 patients. The patho-mechanisms behind the excretion of SARS-CoV-2 remain largely unknown. Federico Coccolini *et al* also demonstrated higher viral load in the peritoneal fluid as compared to the upper respiratory material and are of the opinion that surgical procedures carries a significant risk of transmission of infection. Surgical techniques like electro-cautering, advanced coagulation and cutting devices etc that produce gas and vapor can aerosolize the peritoneal fluid carrying the virus in the surrounding environment. There has been no study till date to show the correlation between respiratory symptoms and the viral load in the peritoneal fluid. Hence all people even with mild respiratory symptoms due to SARS-CoV-2 may harbor a significant viral load in the peritoneal fluid which increases the exposure risk and risk of contagion to

the entire surgical team.

In our innovative technique, we aim to apply the principle of PIPAC therapy and minimize the aerosol exposure to the operating room staff during Laparoscopic Surgery.

PIPAC :

Pressurized Intraperitoneal Aerosol Chemotherapy abbreviated as PIPAC is a procedure where aerosolized chemotherapy is directly injected into the abdomen via a high-pressure injector and appears to be a promising approach for patients with peritoneal malignancy.

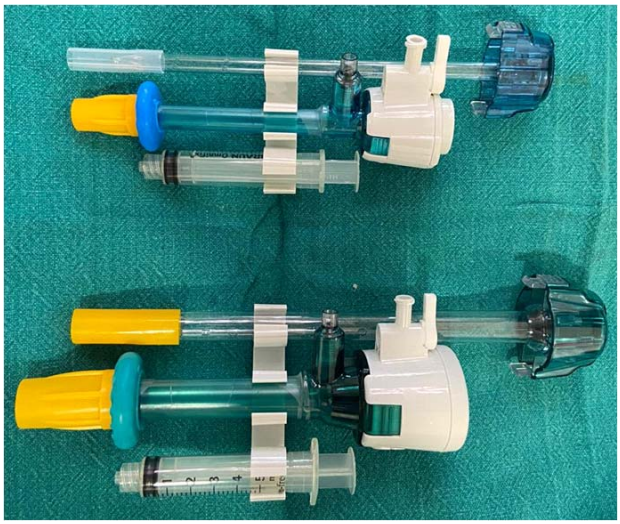

Fig 1 — Ports used in PIPAC (balloon port)

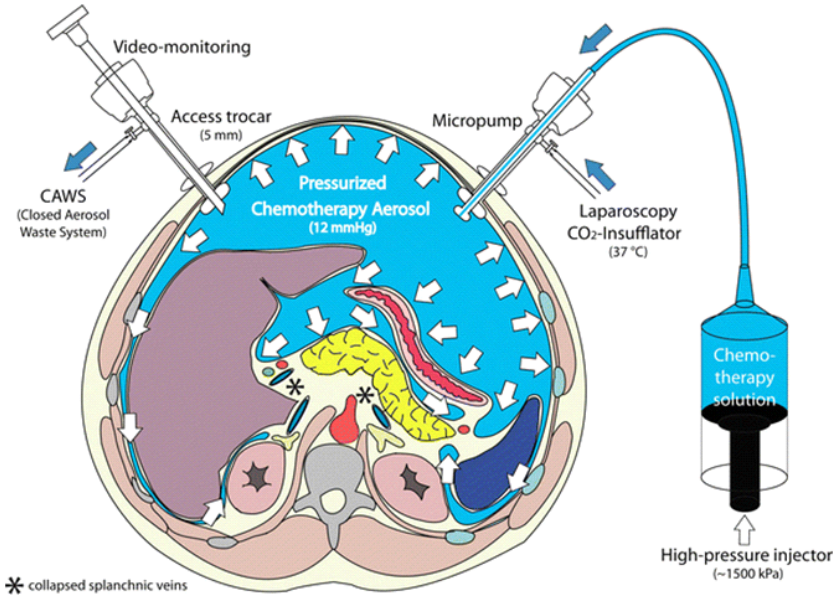

Fig 2 — Schematic representation of PIPAC therapy

[Image taken from Solass W, Kerb R, Mürdter T et al Intraperitoneal Chemotherapy of Peritoneal Carcinomatosis Using Pressurized Aerosol as an Alternative to Liquid Solution: First Evidence for Efficacy. Ann Surg Oncol 2014; ***21:*** *553-9. https://doi.org/10.1245/s10434-013-3213-1]*

PIPAC is performed in an operating room equipped with laminar air-flow. To begin with, a normothermic capnoperitoneum with a pressure of 12 mmHg at body temperature is established followed by insertion of trocars (usually 3). Fig 1 shows the port (balloon port) used during PIPAC. Nebulized with a micropump, the chemotherapy solution (about 10% of a normal systemic dose) is delivered into the tightly closed abdominal cavity in the form of aerosol and is usually maintained for about 30 min.[17] The chemotherapy aerosol is then exsufflated via a closed line over two sequential microparticle filters into the airwaste system of the hospital (Fig 2) followed by retraction of the trocars[18].

Repeated intraoperative analysis of the environmental air showed PIPACto be safe for all staff inside the operation theatre and that it meets the requirements of the German working safety regulations[19].

Application of PIPAC Principle in Laparoscopic Surgery :

The main challenge of Laparoscopic Surgery is the exposure of the surgical team and operating room personnel to aerosol from peritoneal fluid which might occur during cauterization or during exsufflation of the pneumoperitoneum. Hence we thought of applying the principle of PIPAC therapy to Laparoscopic Surgery.

One of the ports (balloon port as used in PIPAC) during Laparoscopic Surgery will be connected to closed aerosol waste system which will be ultimately filtered into the air waste system of the hospital. This will ensure minimum or no exposure of aerosol from peritoneal fluid to the surgical team and other staffs inside the operating room. Fig 3 depicts a schematic model of our proposed system. If applicable this will enable Minimal Access Surgeons to perform Laparoscopic Surgery with minimal risk of exposure during the present COVID-19 pandemic.

Conclusion :

As rightly said the world must move on overcoming all hurdles,so should the Laparoscopic Surgeons continue patient care with minimal

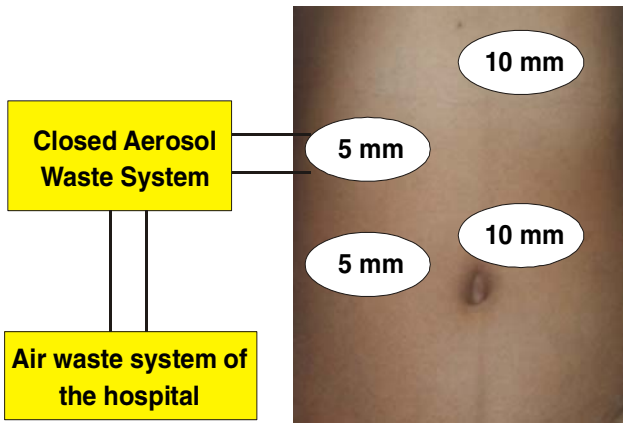

Fig 3 — Schematic representation of laparoscopic surgery procedure with closed aerosol waste system (10mm, 5mm represents the port size)

exposure. Applied properly our proposed model can play a significant role in minimizing exposure to the operating team during the present era of COVID-19.

Limitations : Since this is a proposed model further studies will be required before incorporating it as a practice changing method. Collaboration with centers performing good number of laparoscopic surgeries would help to a great extent in validating our result for the benefit of the large number of Laparoscopic Surgeons Worldwide.

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Review Article

The Tunnel Approach *versus* Medial Approach in Laparoscopic Right Hemicolectomy for Right Colon Cancer : A Retrospective Analysis

Manash Ranjan Sahoo[1], Mahesh Kumar Sethi[2], Kallol Kumar Das Poddar[2]

Background : Laparoscopic right Hemicolectomy for right side colon cancer is well established and proven to be better than open approach in terms of postoperative and overall Hospital stay. Laparoscopic right hemicolectomy can be done by Medial to Lateral, Lateral to Medial or Tunnel (IRETA) approach. No studies have been conducted to compare the clinical outcomes of Medial to Lateral *versus* Tunnel Approach (IRETA) for Laparoscopic Right Hemicolectomy. This study aims to compare the two approaches and explore their advantages and disadvantages.

Methods : This is a retrospective cohort study carried out on 56 patients admitted to department of General Surgery AIIMS, Bhubaneswar hospital from March, 2016 to December 2021 with a diagnosis of right-side colon cancer and underwent laparoscopic right hemicolectomy. They were divided into two groups, group A (n=20) underwent medial to lateral approach and Group B (n=36) underwent Tunnel Approach. Baseline demographics and perioperative parameters were compared between the two groups.

Results : Operative duration, R0 resection and blood loss were significantly lower in Tunnel Approach. Postoperative complications, morbidity, mortality and conversion to open were similar in two groups.

Conclusions : Laparoscopic Tunnel Approach is a feasible and safe procedure and should be the preferred approach in Laparoscopic right Hemicolectomy.

[*J Indian Med Assoc* 2021; **119(10):** 50-4]

Key words **: Tunnel Approach, Medial Approach,**

Carcinoma colon is one of the most common cancers Worldwide, predominantly affecting the old age population. Surgical excision is the preferred treatment for colon cancers. Though the traditional approach for right Hemicolectomy is through Laparotomy, in the era of Minimally Invasive Surgeries, Laparoscopic right Hemicolectomy is being more commonly practised instead open approach. Since the introduction of Laparoscopic right Hemicolectomy by Jacobs in 1990s *et al*[1], it has been established as a feasible and safe procedure to treat right-sided colon cancer with superior short-term outcomes, shorter Hospital stays and lower wound infection rate as compared to the conventional open approach[2,3].

The novel approach in colon cancer Surgeries with Complete Mesocolic Excision (CME) and Central Venous Ligation (CVL) proposed by Hohenberger *et al* in 2009[4], has been widely accepted by most of the Surgeons in many high-volume centers and is believed to be superior to other traditional approaches in terms of local recurrence and cancer related survival. This works on the lines of a similar concept of total Mesorectal Excision (TME) proposed by Prof. RJ Heald[5]. This approach is paramount for efficient lymph node dissection due to high node positive cases in our part of the World, owing to delay in presentation. Laparoscopic CME with CVL approach has been proven to be better than the open approach as far as 5-years survival rate is considered[6]. Its safety and efficacy already have been showed in previous literatures[7].

There are many technical approaches for right Hemicolectomy named as Medial to lateral approach, lateral to Medial approach and the Initial Retrocolic

Editor's Comment :

- Complete Mesocolic Excision (CME) and Central Venous Ligation (CVL) is most efficient approach for lymph node clearance. Laparoscopic CME with CVL has been proven to be better than Open approach.
- IRETA is recently a popular approach for Right Hemicolectomy.

[1]MS, Professor, All India Institute of Medical Sciences, Bhubaneswar 751019

[2]MBBS, Junior Resident, All India Institute of Medical Sciences, Bhubaneswar 751019

Received on : 11/08/2021

Accepted on : 05/10/2021

Endoscopic Tunnel Approach (IRETA). Among them IRETA approach has been recently popularised since the last decade and is increasingly preferred by the Minimally Invasive Surgeons. Many centers have adapted both medial and IRETA approach with their pros and cons. But, the preferred among these two methods in resource limited centers yet to be decided.

Hence, the present study was conducted with the aim to compare the most commonly performed approaches (medial-to-lateral and IRETA) during laparoscopic mesocolic dissection for right sided colonic cancer in terms of overall survival, operating time, intra-operative blood loss, histopathological radicality, conversion to open along with Postoperative recovery and complications in developing countries like in India.

Methodology

A retrospective study was designed with a total of 56 patients with colon cancer who underwent Laparoscopic Radical Right Hemicolectomy Surgery at a single high-volume teaching hospital AIIMS, Bhubaneswar, Odisha, India between January, 2018, to January, 2021. The patients had undergone either IRETA approach (n=36) or Medial to lateral approach (MA) (n=20) as per the surgeon performed during the surgery. Experienced laparoscopic colorectal surgeons performed all the operations. All patient data were collected on demographics, method of Laparoscopic mobilization, intra-operatively duration of surgery and blood loss, histopathological clearance, postoperative recovery and complication and overall survival of the patient.

Inclusion criteria :

(1) All patients with right colon cancer [growth involving caecum, ascending colon and hepatic flexure, or right transverse colon] with age 18 years or more;

(2) Underwent elective Laparoscopic right hemicolectomy with complete mesocolic excision for Tumor;

(3) Tumor not invading adjacent organs.

Exclusion criteria :

(1) Patients age less than 18 years;

(2) Patients who underwent open surgery;

(3) Those who were operated in emergency or for non-malignant etiology;

(4) Patient with distant metastasis confirmed by pre-operative CT scan.

Surgical technique :

All the patients underwent laparoscopic right hemicolectomy and the colon was initially mobilised either medially or initial tunnel approach depending upon the surgeon's choice and expertise. Excised specimen was retrieved via a transverse skin incision in right lumbar region. All patients had stapled extra-corporeal Ileo-transverse side-to-side Anastomosis and received standard postoperative care.

Data analysis :

Data was analysed using SPSS 27.0 (IBM SPSS Inc. Armonk, NY, USA). Comparison between the groups were made using chi-square test or Fischer's exact test as appropriate. Results were extrapolated in Box-and-whisker plot with considering p-value < 0.05 as significant.

Results

A retrospective analysis of the data was performed using SPSS version 27. There is no significant difference in clinicopathological characters of the patients in both the arms, which is depicted in Table 1.

There was a significant difference in the perioperative resection. A total of 14 patients (70%) patient had R0 resection in MA arm and 34 out of 36 in IRETA arm with a p-value of 0.01. Also, there was a significant difference in amount of blood loss as shown in Table 2.

Table 1 — *Clinicopathological Characters*

Characteristics	MA group (N=20)	IRETA group (N=36)
AGE (Years)(mean, SD)	58.39, 6.057	57.70, 6.961
SEX		
Male (%)	9 (45%)	16 (44.4%)
Female	11 (55%)	20 (55.5)
BMI (Kg/m2) (median, IQR)	20.05, 1.8	20.05, 1.27
ASA grade		
I	11 (55%)	18 (50%)
II	9 (45%)	18 (50%)
Site of tumour		
IC Junction	6 (30%)	8 (22.2%)
Cecum	6 (30%)	8 (22.2%)
Ascending colon	5 (25%)	10 (27%)
Hepatic flexure	3 (15%)	10 (27%)
Pre-operative chemotherapy		
Yes	11 (55%)	21 (58%)
No	9 (45%)	15 (42%)
Past history of abdominal surgery		
Yes	11 (55%)	15 (42%)
No	9 (45%)	21 (58%)
Pre-operative CEA (ng/ml)		
<5	12 (60%)	26 (72.2%)
>5	8 (40%)	12 (27.8%)

There were no intra-operative complications like ureteric, duodenal or gonadal vessel injury (Figs 1-4).

Table 3 shows postoperative outcomes and complications. No statistically significant difference was noted.

And after 6 months of follow-up, the Sr.CEA level is significantly lower in IRETA group which signifies adequate tumour resection in IRETA group (Table 4).

Discussion

Although there are many technical approaches for right hemicolectomy, the 'lateral to medial approach' which is the most ancient of them, is mostly preferred

Table 2 — Peri-operative and short-term outcomes

	MA Group (N=20)	IRETA Group (N=36)	P-value
Tumor size (cm) (mean, SD)	7.40, 1.569	7.44, 1.576	0.92*
R0 (no.)	14 (70%)	34 (94.4%)	0.01@
R1 (no.)	3 (15%)	1 (2.8%)	0.125@
R2 (no.)	3 (15%)	1 (2.8%)	0.125@
Blood loss (ml) (median, IQR)	200, 28	120, 23	0.01#
Duration of surgery (min) (median, IQR)	175, 10	160, 10	0.01#
Conversion to open (%) (no.)	3 (15)	2 (5.5)	0.33@
Lymph node yield (no.), (median, IQR)	20, 4	21, 5	0.32#

*: Student t-test, @: Fischer's exact test, #: Mann Whitney U test

Table 3 — Postoperative outcomes & complications

Characteristics	MA group	IRETA group	P-value
First flatus on POD (median, IQR)	2, 1	2, 1	0.4#
Time to oral liquids (median, IQR)	2, 1	2, 1	0.4#
Postoperative hospital stays, Days (median, IQR)	5, 2	5, 1	0.35#
COMPLICATIONS			
Wound infection	1	2	0.3@
Anastomotic leak	0	0	0.55@
Anastomotic stricture	0	0	-
Bowel obstruction requiring re-exploration	0	1	0.35@
Intra-peritoneal infection	1	2	0.3@
Wound/Sheath dehiscence	1	1	0.5@
Paralytic Ileus (IV fluids >7days)	0	0	-

@: Fischer's exact test, #: Mann Whitney U test

Table 4 — *Follow-up after 6 months*

	MA group	IRETA group	P-value
Sr CEA (median, IQR)	6.7, 8.2	4, 5.2	0.04#
Received Adjuvant Chemotherapy	16 (80%)	30 (83.3 %)	0.62@

@: Fischer's exact test, #: Mann Whitney U test

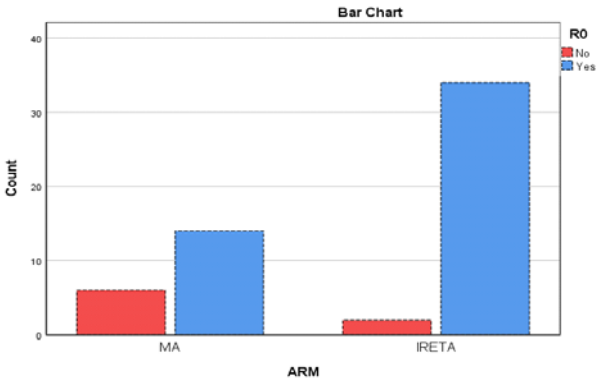

Fig 1 — Histogram showing R0 Resection in both arms

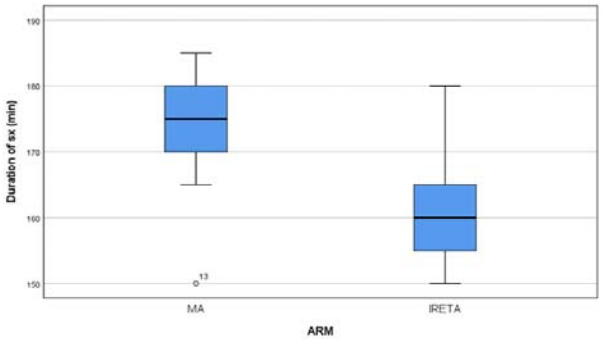

Fig 2 — Box-whisker plot showing duration of surgery across both the arms

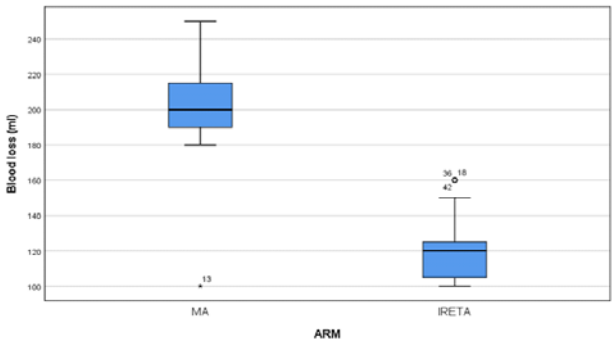

Fig 3 — Box-whisker plot showing blood loss across both arms

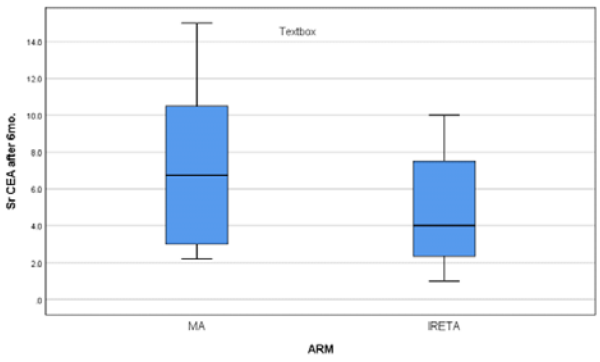

Fig 4 — Box-whisker plot showing Sr CEA after 6 months across both the arms

in open approaches[15,8]. It starts with division of the lateral peritoneal attachments followed by an exploration of medial mesenteric attachments and division of the blood vessels[9,10].

This was followed by development of 'the medial to lateral approach' by Milson and colleagues, which explains a vessel first approach from medial side followed by division of the lateral peritoneal attachments[11,12]. This was widely accepted because of its pedicle/vessel first approach with "no-touch" principle followed by mesocolon mobilization. Many previous studies have collated its safety and efficacy compared with the former approach[13,14] which shows superiority of MA approach in terms of less duration of Surgery and less blood loss.

In our study, we have compared the Medial to Lateral Approach (MA) to Initial Retrocolic Endoscopic Tunnel Approach (IRETA). There was a significant difference in intra-operative blood loss (200, 28ml in MA approach *versus* 120, 23ml in IRETA approach, p-value=0.01). Also, there was a significant decrease in duration of surgery in IRETA approach (175, 10min in MA approach *versus* 160, 10min in IRETA approach, p-value=0.01). But, at times MA approach might be troublesome if there is local infiltration of the tumour and it may cause difficulty in getting into the fascial plane via mesenteric window, especially in obese patients[7]. It also has a steep learning curve and higher conversion rate to open as its drawbacks as shown in two previous studies[15,16].

Recent studies have shown extended lymph node dissection with CME to have better oncological outcomes, without any significant difference in complications[17,18]. Over the last decade, development of retrocolic tunnel approach which involves initial retroperitoneal mobilisation between parietal and visceral fascia of mesocolon, followed by dissection vertically along superior mesenteric vessels, ileocolic, right colic and right branch of middle colic vessels, has become the preferred approach worldwide in many high-volume centres.

The Initial Retrocolic Endoscopic Tunnel Approach (IRETA) is a stepwise approach that provides excellent view and easy identification of retroperitoneal structures and clearance of fibro fatty and lymphatic tissue along the vessels and also an easy approach to high ligation of the vessels. Even though a minimum retrieval of twelve lymph nodes is considered to be adequate for lymphatic dissection, previous studies have demonstrated numbers ranging from 19 to 32[8,19] in IRETA approach. In our study, we retrieved a median of 20,4 lymph nodes in MA approach *versus* 21, 5 lymph nodes in IRETA approach with no significant difference.

With IRETA approach, the retroperitoneally placed ureter can be safely dissected off from the tumour irrespective of the size and it also minimizes tumour handling eventually minimising risk of bowel injury and tumour seeding[8,20]. In our study, there were no ureteric injury, bowel injury or gonadal vessel injury. IRETA approach also eases the surgery with significantly minimising the amount of blood loss and operative duration, both of which were also evident in our study also. Its primary utility is in large tumors where CME is essential to maximise the Oncological outcomes. In our study, it also showed a significant difference in number of R0 resections (34/36 in IRETA approach *versus* 14/20 in MA approach, p-value=0.04).

Conclusion

Laparoscopic initial retrocolic endoscopic tunnel approach for right colon cancer is simple to implement, safe and feasible with improved intra and postoperative outcomes when compared to the conventional medial to lateral approach. It is more applicable in tumours presenting late and bulky tumors where adequate lymph node dissection and R0 resection is challenging.

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Case Report

Double Cystic Duct : Case Report of a Rare Presentation in a Common Operation

Anshuman Poddar[1], Om Tantia[2], Shashi Khanna[3]

Variations of cystic duct anatomy are not uncommon and are continuously encountered during imaging and surgery. Failure to identify these variations may result in complications during Surgical, Endoscopic, Percutaneous Intervention Procedures. Though variation of the cystic duct anatomy is common but it's duplication is a very rare entity with about 16 cases reported so far. The diagnosis may be missed by imaging studies including MRCP.

Here we present a case of double cystic duct arising from a single Gall Bladder in a 54-years female patient admitted for Cholecystectomy at ILS Hospitals, Kolkata. She underwent Laparoscopic Cholecystectomy which revealed the presence of H type of double cystic duct. It was confirmed by intra-operative cholangiography. Both the cystic ducts were dealt appropriately and the patient had an uneventful postoperative recovery. She is being followed up regularly and is healthy.

In conclusion, duplication of the cystic duct is a very rare occurence.it's pre or intraoperative identification is important to avoid ductal injury.

[*J Indian Med Assoc* 2021; **119(10):** 55-7]

Key words **: Double cystic duct, CBD injury, Laparoscopic cholecystectomy, Anatomic variations of cystic duct.**

Variations of Cystic Duct (CD) anatomy are not uncommon and are continuously encountered during imaging and surgery. Failure to identify these variations may result in complications during Surgical, Endoscopic or Percutaneous Intervention procedures. Hence a proper knowledge and pre-operative or intra-operative identification of these variations are of utmost importance to prevent the incidence of Common Bile Duct (CBD) injury during cholecystectomy.

Though cystic duct variation is common, duplication of cystic duct is an extremely rare variant with only 16 cases reported in literature[1]. The diagnosis can be missed by imaging studies and is generally identified intraoperatively[2]. However, it may go unidentified during the surgery and is then identified in the postoperative period during a diagnostic work up for patients presenting with persisting biliary symptoms[3].

Here we present a case of Double Cystic Duct (DCD) arising from a single Gall Bladder in a 54-year female patient admitted for Cholecystectomy at ILS Hospitals, Kolkata.

Department of Minimal Access & Bariatric Surgery, ILS Hospital, Kolkata 700064

[1]MBBS, MS, Consultant

[2]MS, FRCS (Eng), FICS, FAIS, FMAS, Medical Director & Head and Corresponding Author

[3]MBBS, Consultant

Received on : 08/04/2021

Accepted on : 25/09/2021

Editor's Comment :

- Variations in the anatomy of cystic duct is not uncommon.
- A surgeon should be well versed with them for avoidance of injury to the common bile duct.
- Proper pre-operative investigations including imaging studies should be done for its identification, if any doubt arises intra-operatively, an IOC should be performed.

Case Report

A 54-year-old female presented with complaints sharp pain in the epigastric region which was radiating to right shoulder. The pain was associated with nausea. The patient was diagnosed as Gall Stone pancreatitis and was admitted for cholecystectomy.

On examination she had severe epigastric tenderness. All the vital signs were stable and there was no other significant finding[3].

Routine pre-operative investigations were essentially normal. USG of the abdomen showed multiple Gall stones, and the CBD was normal in Caliber with a diameter of 6 mm. Magnetic Resonance Cholangio-pancreatography (MRCP) revealed Calculous Cholecystitis, prominent proximal common bile duct without obvious luminal altered signal intensity. There was no sign of double cystic duct in MRCP.

Patient underwent standard four port laparoscopy which revealed thick walled gallbladder with dense adhesions. Adhesiolysis was done.Calot's triangle dissection showed Double Cystic Duct with single cystic artery. Presence of double cystic duct was confirmed by

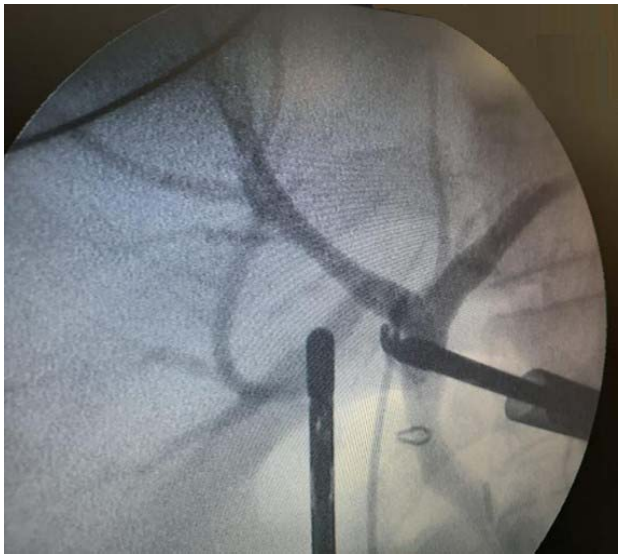

Fig 1 — Intra-operative cholangiogram of double cystic duct

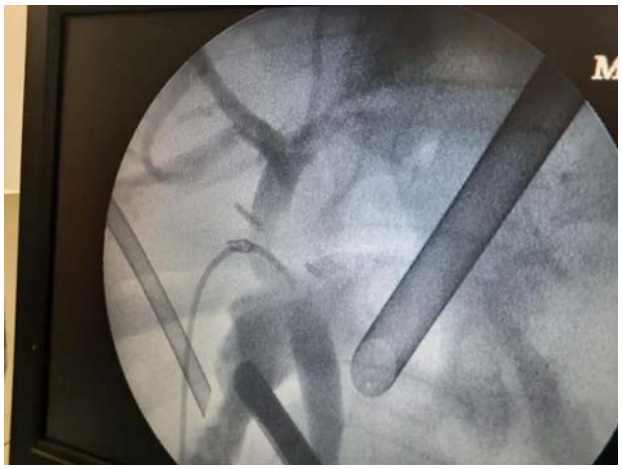

Fig 2 — Intra-operative cholangiogram of double cystic duct

Intra-operative Cholangiography (IOC) (Figs 1 and 2). One cystic duct was clipped with hemolock and the 2nd cystic duct, seen to be draining into the right hepatic duct, was short in length and hence sutured with 3-0 vicryl. Macroscopic examination of the specimen showed the presence of double cystic duct (DCD). The patient was discharged in a stable condition after 48 hours.

The patient is being followed up regularly and she is stable and healthy. Histopathological examination revealed chronic cholecystitis.

Discussion

Variations in the anatomy of the cystic duct, especially DCD, intraoperatively during cholecystectomy is a matter of concern for the surgeons. Variation of cystic duct anatomy is not rare[4]. A standard anatomical relation between the extrahepatic bile duct, cystic duct and arteries is seen in only 1/3rd of the individuals. In 2/3rd of the patients, the cystic duct enters into the Common Bile Duct (CBD) in an angular fashion. In about 1/5th cases the cystic duct runs parallel to the CBD and it's the entry into the CBD is straighter. In less than 10% cases the cystic duct runs spirally taking a tortuous course and connecting the CBD at different angles. In less than 1% of the patients, it is seen to be draining directly to the right hepatic duct. Presence of two cystic ducts ia a very rare event[2]. It is seen more commonly in the females with an incidence of 73%[1]. No age is exempt from this and its time of presentation can range from new born to 76 years old[5,6]. Our case was a 54-year-old female. Vincente *et al* reported a case of a neonate with VACTERL anomaly showing the presence of DCD during cholecystectomy for symptomatic cholelithiasis[6]. Otaibi *et al* showed the presence of double Gall Bladder in DCD in 80% of the cases[7]. However, about 1/3rd of the reported cases of DCD are associated two Gall Bladders. In our case we did not find any accessory Gall Bladder and both cystic ducts drained from same Gall Bladder (Fig 3). The classification of DCD byFlannery and Caster according the configuration of the ductsis as follows. The "H type" is the commonest type where the second cystic duct drains separately into either the left, right or Common Hepatic Duct (CHD). In the"Y type" variant, both the cystic ducts first unite to form a common duct which then drains into the common hepatic duct. The trabecular type is the where the accessory duct drains directly into the Liver Substance[8]. Our patient had an H type variant of DCD with one duct draining in the CBD and the second duct draining into the RHD. Pre-operative diagnosis of DCDis

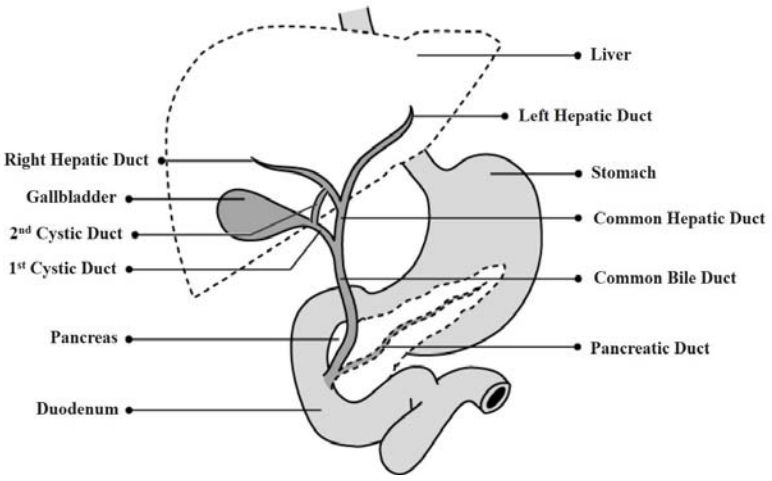

Fig 3 — Schematic Representation of Double Cystic Duct

very difficult due to the rare nature of this variation and also there is difficult identification of the two ducts radiologically.

Both ultrasound of the abdomen and MRCP failed to reveal the presence of DCD in our case. Some surgeons like to go for routine use of intraoperative cholangiography to delineate bile duct anatomy which prevents injury to the CBD that might occur because of the presence of different variations of the cystic duct anatomy.

Conclusion

Duplication of the cystic duct is a very rare occurence. It's pre or intraoperative identification is important to avoid ductal injury.

Funding : NA

Conflicts of interest/Competing interests : The authors declare that they have no potential conflicts of interest to disclose.

Ethics approval : The ILS Hospitals Ethics Committee declared after consultation that this manuscript does not require IRB approval.

Consent to participate : NA

Consent for publication : NA

Availability of data and material : The data and material provided in the case report is transparent & true as per the knowledge of the authors.

Code availability : NA

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Case Discussion in Medicine

Low Back Pain for Clinicians : An Evidence Based Approach

Shounak Ghosh[1], Alakendu Ghosh[2]

Low back pain is one of the most common causes of disability and missed workdays across the Globe. Symptoms may range from non-specific mild complaints like stiffness to frank inability to perform daily activities and with an increase in sedentary lifestyle and aging, the prevalence of such complaints is expected to increase. A thorough history and physical examination are essential for the evaluation of low back pain, especially in the primary care setting with diagnostic tests based on specific findings and response to initial therapy. The localisation of pain and its associated "red flags" may provide important clues for patient referral and treatment. Pharmacologic, non-pharmacologic and surgical options may all be tried, depending on the nature and cause of pain and disability. Several Clinical Practice Guidelines have been proposed for highlighting a feasible approach to the management of both acute and chronic low back pain.

[*J Indian Med Assoc* 2021; **119(10):** 58-62]

Key words **: Low back pain, Red flags.**

"The greatest evil is physical pain"
— Saint Augustine

Low back pain is a common medical condition and among the most common causes of disability Worldwide, even if the underlying cause may not always be a grave one. Surveys have revealed it as the second most common symptomatic reason for physician visits[1] and only up to half the number of patients seek medical care as most of the cases are self-limiting. Global epidemiologic studies have estimated the point prevalence to range from 15-30%[2], while recent Indian data reveals a similar figure of 32%[3] in a North-Indian setting. The associated economic burden is quite significant, including both costs of direct medical care or physiotherapy, as well as the indirect expenses incurred from losing out on work and facing disability.

While the bulk of low back pain as a presenting complaint is faced in a primary care setting, various aspects of management are shared amongst physicians, neurologists, rheumatologists, emergency care practitioners as well as non-allopathic healthcare providers like chiropractors and physiotherapists. Symptomatic outcomes are marginally better with intensive treatment, but not all patients require a detailed diagnostic workup or long-term management.

Editor's Comment :

- LBP is the commonest symptom people experienced in their life time.
- Non-inflammatory etiology is the predominant component.
- Imaging modality like MRI is to be used in the selected population where "red flag sign" is there.
- Non inflammatory group require supportive care with physiatrist modulation where as inflammatory pain require NSAID as disease modifying drugs followed by synthetic biologic DMARD.

Recognizing early indicators of poor prognosis smoothens the transition to pain-free or disability-free living.

Among the guidelines for managing low back pain, the UK National Institute for Health and Care Excellence (NICE) clinical guideline for low-back pain and sciatica from 2016[4] and the clinical practice guideline from the American College of Physicians (ACP) from 2017[5] have been used to provide evidence for this review discussing the primary management and supportive care for low back pain.

Aetiology & Definitions :

Low Back Pain (LBP) refers to pain experienced in the lumbosacral or spinal regions with or without neural compromise or visceral referred pain. The differential diagnoses for low back pain have been elaborated in Table 1 and may be divided into the following groups: mechanical (spinal), non-mechanical (spinal) and visceral/miscellaneous. The Quebec Taskforce Classification for Spinal Disorders[6] has defined the duration of acute (2– 4 weeks), subacute (≤12 weeks) and chronic (typically ≤12 weeks) LBP and the pathophysiologic pathways or exact cause for any of these may not be entirely clear. Causes like disc

[1]MD, DNB (Rheumatology), Resident, Medanta–the Medicity, Gurgaon, Haryana 122001

[2]DNB, FRCP (London), Former Head, Department of Clinical Immunology and Rheumatology, IPGME&R and SSKM Hospital, Kolkata 700020

Received on : 23/08/2021
Accepted on : 01/09/2021

Table 1 — *Differential Diagnosis of low back pain (modified from Atlas and Deyo[7])*

Mechanical Spinal Causes	Non-mechanical Spinal Causes	Visceral and Miscellaneous
Idiopathic (lumbar strain/ ligamentous)	Neoplastic	Gastrointestinal
Degenerative	• Metastases	• IBD
• Disc	• Myeloma	• Pancreatitis
• Facet joints	• Lymphoma	• Diverticulitis
• DISH	• Primary spinal cord tumor	Renal
Spondylosis	Infective	• Pyelonephritis
Spondylolisthesis	• Osteomyelitis	• Nephrolithiasis
Spinal canal stenosis	• Discitis	Vascular
Disc herniation/disruption	• Epidural abscess	• Abdominal Aortic aneurysm
Vertebral fracture	Inflammatory	• AortoarteritisPelvic
Congenital	• Ankylosing Spondylitis	• Endometriosis
• Kyphosis	• Psoriatic Arthritis	• PID
• Scoliosis	• Reactive Arthritis	Fibromyalgia
• Transitional vertebra	Paget's Disease	Somatoform disorder
	Scheuermann's Disease	

(DISH : Diffuse Idiopathic Skeletal Hyperostosis; IBD : Inflammatory Bowel Disease; PID : Pelvic Inflammatory Disease)

herniation can be a persistent anatomical and mechanical cause of nerve root irritation, while some inflammatory conditions can lead to the dysregulated modulation of pain-processing nerve fibres and be harder to localize or treat.

Some of the common conditions or symptoms related to LBP are as follows:

- Sciatica: Leg pain localizing to lumbar sacral nerve roots, usually of the L4 to S1 levels.
- Spondylolisthesis: A vertebra slipping out in relation to the vertebra beneath it.
- Spondylolysis: A defect in the pars interarticularis; commonly seen with stress fractures and back pain.
- Spondylosis: Degenerative arthritis of spine.
- Disc Protrusion & Bulge: In protrusion, the nucleus pulposus pushes completely through the annulus and squeezes out of the disc. In a bulge, the bulged disc material is still contained within the annulus. If a piece of the disc is broken, it's called a sequestered fragment.
- Cauda Equina Syndrome: Compression of the cauda (bundle of nerve roots in the lower spinal canal). This may cause bowel or bladder issues or saddle anesthesia.
- Spinal Stenosis: Crowding of spinal canal, either by osteoarthritis, osteophytes or ligamentous thickening. The narrowing of the canal can cause nerve root compression.
- Myelitis: An inflammatory condition of the spinal cord. Frequently, white matter and demyelination are involved.
- Conus Medullaris Syndrome: Lesions where the spinal cord tapers and ends, between the first and second lumbar vertebrae and may cause increased tone and reflexes

History & Physical Examination :

Acute LBP usually has an underlying mechanical cause like trauma or vigorous exercise. The nature of pain may be described by the patient as "shooting" in radiculopathy or "throbbing/aching" in musculoskeletal causes. Radiation of pain may Reveal Radiculopathy or Visceral Referred Pain Syndromes and differentiating neuropathic pain is important while deciding on treatment protocols.

The main aim of initial evaluation is to stratify patients into 3 major groups:

- Patients with "red flag" signs: Major underlying illness requiring further investigations or referral, seen in a minority of cases (Table 2)
- Patients with Nerve Root Involvement (Radiculopathy): A thorough examination including site of radiation, local deformities of spine, areas of motor and sensory involvement (Table 3), diminished deep reflexes or worsening on sneezing/straight leg raising.
- Non-specific back pain: Majority of patients are of this category with milder symptoms.

A detailed examination should include a thorough nervous system examination, as well as other systems to check for underlying causes. The Waddell manoeuvres may be used for suspected cases of non-organic back pain (Fig 1). Forward and lateral flexion of the spine, gait abnormalities and focussed joint examination may point towards the causative disease process (Table 4).

One should always look out for "Yellow flags" (psychological behavioural factors: beliefs and coping strategies about pain and support) "Blue flags" (socio-economic factors: work status and health insurance benefits), and "Black flags" (occupational factors: working conditions and policies) associated with LBP

Table 2 — *Red Flag features in Low Back Pain*

Feature	Suspected Condition(s)	Associated findings
Age >50 years	Malignancy; Osteoporosis	Constitutional features (weight loss), bleeding, lymph nodes, smoking; Trauma, postmenopausal female, contraceptive or steroid use
Age <20 years	Congenital (Spina bifida, kyphosis, epiphyseal dysplasia)	Family history, other birthmarks or anomalies, neurologic symptoms
Constitutional features (Fever, weight loss)	Malignancy; Infections	Features of primary organ involvement, anemia, bleeding;Features of meningitis, associated neurologic deficit
Inflammatory LBP	Ankylosing Spondylitis; Psoriatic Arthritis; Reactive Arthritis; Arthritis associated with IBD	Age <40 years (especially men), morning stiffness >30 min, improvement with exercise and NSAIDs, duration >3 months
Neurologic deficit	Myelopathy; Radiculopathy	Sudden onset weakness, bladder or bowel involvement, sensory loss, diminished reflexes
Immunosuppressive or steroid use, Drug use/HIV	Vertebral fracture; Infections	Focal tenderness, neurologic deficit, deformity, worse on movement; Constitutional features

Table 3 — *Neurologic findings in Nerve Root affection*

Nerve Root	Motor Weakness	Sensory Affection	Reflex
L2	Hip flexion & adduction	Anterior thigh	Cremasteric
L3	Quadriceps adductors	Anterior & medial thigh	Patellar
L4	Knee extension, hip flexion	Anterior thigh, medial malleolus	Patellar
L5	Great toe dorsiflexion	Dorsal foot, lateral leg	None
S1	Plantar flexion	Lateral foot, heel Posterior leg	Achilles

to facilitate rehabilitation later.

Diagnostic Testing :

Imaging :

Imaging modalities are often performed in the evaluation of LBP but are seldom necessary or useful. Guidelines do not recommend the use of imaging for non-specific back pain (>85% cases). Moreover, >30% adults without symptoms of LBP may have positive imaging findings like Degenerative Disc Disease[9], thus leading to more confusion than clarity in management.

Plain radiographs may be a satisfactory modality to reassure patients of the absence of any obvious or major spinal pathology but the yields from such radiographs are too low to justify their routine use, unless there are risks of vertebral fracture or persistent, refractory LBP. Both anteroposterior and lateral views may be required in such cases.

In case of strong suspicion of cord pathology, nerve root

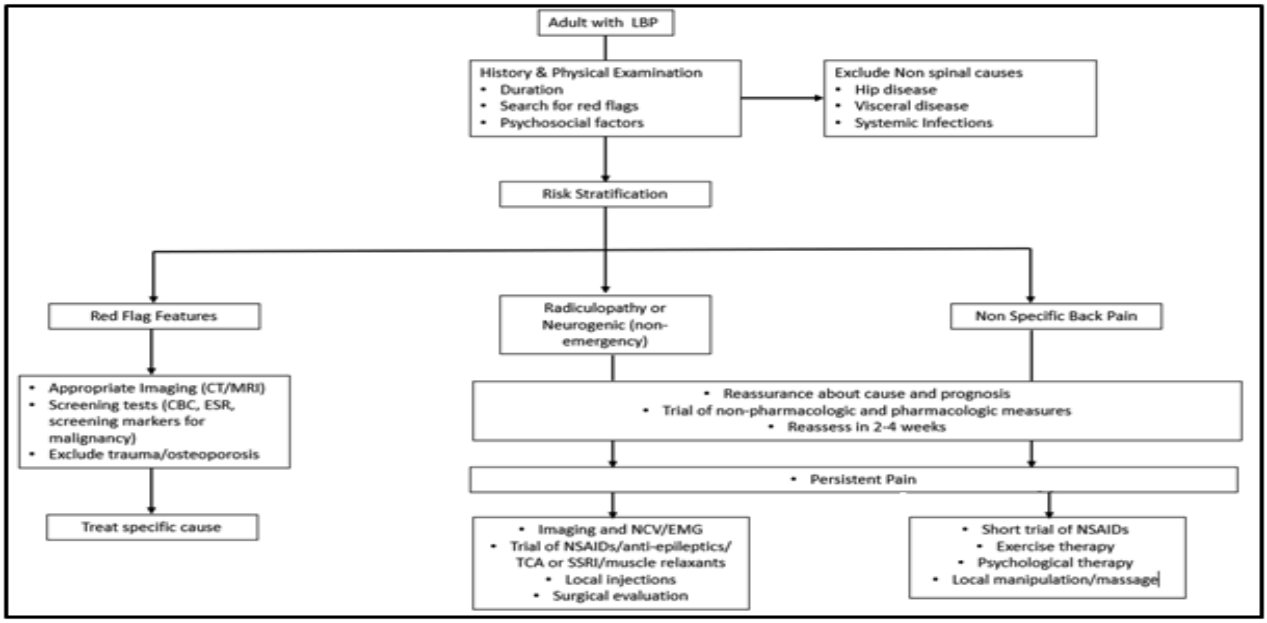

Fig 1 — Algorithm for Approaching Low Back Pain

Table 4 — *Waddell Signs[14] for Non-organic LBP*

Category	Signs
Tenderness	• Superficial Skin tender to light touch • Non-anatomic deep tenderness not localized to one area
Simulation	• Axial loading of spine over skull of standing patient elicits low back pain • Roation : shoulders and pelvis rotated in the same plane elicits low back pain
Distraction	• Differences in supine straight-leg-raising and seated straight-leg-raising
Regional	• Weakness : many muscle groups give away weakness (patient does not give full effort on minor muscle testing) • Sensory : sensory loss in stocking or glove distribution; non-dermatomal
Overraction	• Disproportionate facial or verbal expression (ie, pain behavior)

involvement or suspected malignancy, advanced imaging techniques like Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) should be advised, especially for persistent symptoms of radiculopathy or spinal stenosis despite empirical treatment. MRI is often preferred by physicians as it is comparable to CT in diagnosing Spinal Degenerative Diseases, while being more sensitive in the diagnosis of any other inflammatory, vascular or soft tissue pathology[9], without the risk of radiation exposure. Inflammatory low back pain may be diagnosed as sacroiliitis early using MRI to show erosions or bone marrow edema. Most guidelines recommend the use of imaging in the presence of either red flag features or pain persisting beyond 4-8 weeks with conservative management.

Electrodiagnostic Studies :

Nerve Conduction Studies (NCV) or Electromyography (EMG) may be used to confirm the diagnosis in cases of suspected sciatica, Radiculopathy or Neuropathy. Inflammatory Muscle Diseases may be picked up on EMG as persistent LBP with thigh pains and weakness. The sensitivity of EMG has been shown to be comparable to CT or MRI in localizing radiculopathy[10] but sensory root injury cannot be ascertained by it.

Treatment :

Most cases of acute LBP may be self-limiting, and non-specific pain may be managed primarily by reassurance or lifestyle changes. A multidisciplinary approach is advocated by all the Clinical practice guidelines for managing LBP. An algorithm to approach and manage LBP has been summarised in Fig 1.

Acute LBP management :

Guidelines recommend early, active ambulation over bedrest for acute LBP with reassurance about good prognosis, limiting the need for bedrest only for severe disabling pain or injury. Non pharmacologic management is usually preferred. There is low quality of evidence favouring the use of massages and manual spinal manipulation, but they both have been recommended for use in the NICE as well as the ACP guidelines for acute LBP.

Psychological and cognitive-behavioral approaches are recommended as part of a broader treatment plan. ACP (not NICE) recommends the use of acupuncture and local heat application in cases of acute LBP but there is only low quality of evidence and there is not enough evidence to support stimulation techniques like Transcutaneous Electrical Nerve Stimulation (TENS) due to lack in RCT data.

NSAIDs have been recommended for the shortest possible duration. Opiods are endorsed by the NICE guidelines while short duration use of muscle relaxants are recommended as second line therapy by the ACP but with low quality evidence in their favour. Corticosteroids are not recommended by any of the guidelines.

Chronic LBP Management :

Data from RCTs provide evidence that exercise therapy, cognitive behavioural therapy or spinal manipulation may be preferred for managing persistent non-specific LBP. Therapeutic Ultrasonography or TENS-like techniques have not shown meaningful results in altering the outcome in chronic pain.

While the use of NSAIDs over placebo is recommended by both US and UK, other modalities like anti-depressants, muscle relaxants or epidural or facet joint steroid injections have not shown significant benefits and are not recommended based on this insufficient evidence[12].

Specific Management :

Radiculopathy requires a multidisciplinary approach, including active exercise therapy and the use of anti-epileptics like Gabapentin, Pregabalin and Topiramate are recommended by most existing guidelines based on moderate quality of evidence.

Tricyclic anti-depressants (eg: Amitriptyline) or Selective Serotonin Reuptake Inhibitors (SSRIS) like Duloxetine are recommended in both sciatic pain or for features of chronic pain syndrome not responding to non-pharmacologic measures. Even opiods may be used for refractory cases.

Epidural steroid injections (NICE endorsed) or

surgical procedures like discectomy may be recommended in cases with nerve compression.

Referrals for surgery, rehabilitation or psychological therapy are often based on questionnaires used by physicians as screening tools but the accuracy of these tools are modest at best[13]. Decisions of referral are best tailored to the individual patient based on a combination of clinical or imaging findings, to facilitate any urgent interventions as and when needed.

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Short Communication

Are COVID-19 Survivors Likely to be Better Poised to Prevent Cancer or to Cope with it ? — A Contesting Viewpoint

Shambo S Samajdar[1], Saibal Moitra[2], Shashank R Joshi[3], Santanu K Tripathi[4]

The global community was witnessing a new World War, quite distinct from the World War I and World War II. The battle against the whole human race was waged by a tiny RNA virus – named SARS-CoV-2. The disease it causes is named COVID-19. First identified in Wuhan province of China in December, 2019, the disease had been spreading like a wild fire almost all around the globe. The World Health Organization declared it a pandemic on 11th March, 2020. The disease has an incubation period of 3-7 days and the longest time from infection to symptoms is 12.5 days (95% CI, 9.2 to 18)[1]. The infection has a high transmission rate; on an average, an infected person transmits the infection to an additional 2.2 individuals[2]. The size of infected cohort in this novel epidemic is known to be doubled about every 7 days. In just around 100 days, SARS-CoV-2 has already affected more than 120 million people in 210 countries, and has claimed more than 2.6 million lives. Described as the worst ever crisis the human civilization had confronted with, it had caught the modern medicine and healthcare system unaware and clueless. Though we have vaccines now to fight against the epidemic, but mutating strains are the major concerns for scientists. Second wave of the epidemic already started devastating a few countries and India is in the verge of it.

The case fatality rate of SARS-CoV-2 infection albeit relatively low – around 3 per cent, as compared to SARS-CoV-1 or MERS-CoV, its high transmission rate translating to the huge absolute number of deaths, has been the real cause of concern. The severity and death in COVID-19 is attributed to a deadly uncontrolled systemic inflammatory response – a cytokine release syndrome (CRS) and cytokine storm, causing acute respiratory distress syndrome (ARDS). There is release of large amounts of pro-inflammatory cytokines (IFN-á, IFN-ã, IL-1â, IL-6, IL-12, IL-18, IL-33, TNF-á, TGFâ, etc.) and chemokines (CCL2, CCL3, CCL5, CXCL8, CXCL9, CXCL10, etc) by immune effect or cells in severe COVID-19 patients. High levels of pro-inflammatory cytokines lead to shock and end-organ damage, specifically Acute Respiratory Distress Syndrome (ARDS). Autopsy findings suggest evidence of tissue necrosis and interstitial macrophage and monocyte infiltrations in the lung, heart and gastrointestinal mucosa, signifying elevated inflammatory cytokines[3,4]. In critical COVID-19 patients, it is commonly seen that they have severe lymphopenia with hyper activated pro-inflammatory T cells[5] and decreased T-reg cells[6].

Many risk factors have been recognized that might increase the susceptibility as well as the vulnerability to SARS-CoV-2 infection and the poor prognosis of COVID-19. Cancer in general is believed to adversely affect the outcome in COVID-19 patients. One study showed prevalence of cancer was 1% (95% confidence interval, 0.61%-1.65%) among COVID-19 patients in China[7], whereas another suggested that the pooled prevalence of cancer was 2.0% (95% CI, 2.0%-3.0%). These data came from a meta-analysis of 11 reports including 3,661 COVID-19 cases[8]. On the other hand, to the best of our knowledge nothing is yet known how SARS-CoV-2 infection can affect different malignancies, in terms of their covert and overt progression. We herewith put forward our viewpoint based on our understanding of how the SARS-CoV-2 infection modulates the innate and adaptive immunity in humans.

Treatment modalities in cancer are evolving and immunotherapy is today addressed as the fifth pillar of cancer care, after surgery, radiotherapy, cytotoxic chemotherapy and molecular targeted therapy[9]. Chimeric Antigen Receptor (CAR) T-cell is a developing Cancer Immuno-therapy. After collecting a patient's own immune effector cells like T cells or NK cells, these are genetically engineered to express a chimeric antigen receptor which recognize a tumor-related target, expanded in vitro, and then reinfused to produce responses. This therapy prevents progression in a variety of malignancies[10]. In 2010, the first report of CAR T-cell therapy was published, in a patient with

[1]MD, DM Clinical Pharmacology, School of Tropical Medicine, Kolkata 700073 and Corresponding Author

[2]MD (Respiratory Medicine), PhD, FCCP(USA), DAA(CMC), Consultant Pulmonologist and Professor, Department of Allergy & Immunology, Apollo Gleneagles Hospitals, Kolkata 700054

[3]MD DM(Endocrinology) FICP, FACP(USA), FACE(USA), FRCP(Lon,Glsg & Edin), Consultant Endocrinologist, Joshi Clinic, Mumbai & Dean, Indian College of Physicians, Mumbai 400050

[4]MD, DM Clinical Pharmacology, Ex-Professor and Head, Department of Clinical Pharmacology, School of Tropical Medicine, Kolkata 700073

Received on : 20/03/2021
Accepted on : 05/10/2021

advanced follicular lymphoma; after infusion of CAR T-cells engineered to target CD19 protein, there was dramatic regression of lymphoma[11]. Beneficial effects were seen in acute lymphoblastic leukemia (ALL), Chronic Lymphocytic Leukemia (CLL), and many types of non-Hodgkin lymphoma (NHL)[10]. CAR T Cell therapy is associated with a dreadful adverse effect – the CRS. It is due to results of large amounts of cytokines, including IL-6 and interferon ã rapid release into the bloodstream by activated CAR T-cells[12]. Clinical trials have shown very promising results in end-stage patients of acute lymphocytic leukemia with a full recovery of up to 92%[13].

At this juncture the questions that intrigue us are, whether the patients who recovered from the cytokine storm will be less susceptible to some cancers in future, and whether the patients' micro-cancer cells can be damaged by this virus-made disaster. We make an attempt here to find an empiric answer to these questions, in the backdrop of the apparent analogy of immunopathogenesis of COVID-19 (as described above) and the rational basis of cancer immunotherapy.

The basis of cancer immune-therapeutics is activation of Cytotoxic T Lymphocytes (CTL) to kill the cancer cells. The T regulatory (T-reg) cells help cancer cells to be saved from the attack of CTLs. In severe COVID-19, the activity of T-reg cells is found to be decreased. The CTL-associated antigen 4 (CTLA 4) and programmed cell death protein 1 (PD1) are important negative regulators of T cell immune function. Immune check point inhibitors (ICI) like CTLA 4 inhibitors (namely, ipilimumab) and PD1 inhibitors (namely, pembrolizumab), are known to increase anti-tumor immunity and have durable clinical response. As they block CTLA 4 and PD1, the CTLs become activated, and the interaction of co-stimulatory receptor and ligand in antigen presenting cell (APC) is enabled. This makes the cancer cells more susceptible to be destroyed by immune cells. CTLA 4 inhibitors also help to inhibit T-reg cells mediated suppression of CTLs. CTLA 4 inhibitors are successfully used in non-small cell and small cell lung cancers, Hodgkin lymphoma, bladder cancer, renal cell carcinoma, melanoma, and Merkel cell carcinoma[14]. The ICIs also carry the risk of pneumonitis and cytokine storm and the mechanism is same like COVID-19. IL 6 inhibits T-reg cell differentiation via CD4 T lymphocyte modulation, and increases cytotoxic T lymphocyte proliferation via CD8 T cell stimulation[15]. Given the fact that IL-6 is a cytokine with its multi-faceted, non-specific immune-modulatory role in humans, it may not be too far-fetched to assume that it can confer some immunity to development of or progression of cancer. To examine this hypothesis, we recommend conduct of well-designed prospective, observational study with three matched (in terms of cancer risk factors) cohorts – one critical COVID-19 survivors, one non-critical COVID-19 patients after recovery, and another non-COVID-19 participants, and following them up for assessing the relative risk of cancer among them. One can also take up cancer genomics research in suitable animal models like with knockout mice for the genes involved in cancer regulation.

All crises bring with them a host of opportunities. We need to think through the crisis of COVID-19, particularly the molecular basis of its immune-pathogenesis and manifestations and understand its nature thoroughly. May be, we shall be rewarded with the much sought-after solution to the problem of cancer immuno-modulation.

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Image in Medicine

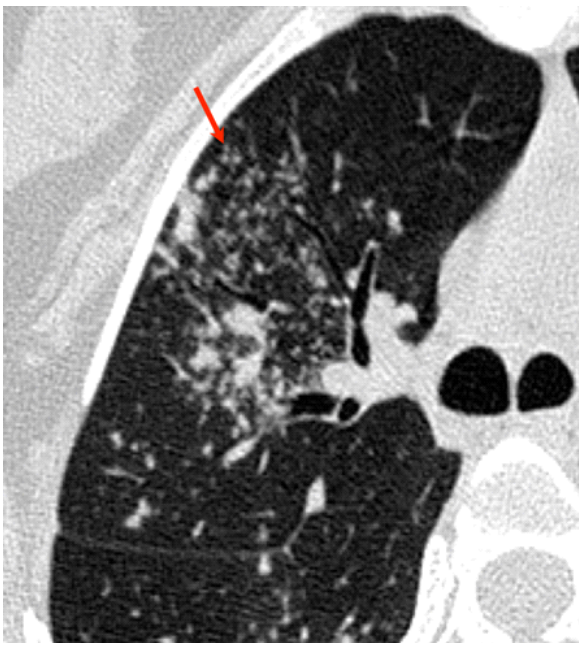
Bhoomi Angirish[1], Bhavin Jankharia[2]

Quiz 1

CT scan images of the chest of a 24 year old male presenting with cough and weight loss.

Questions :

(1) What is the diagnosis?
(2) What is the pathophysiology of this pattern?
(3) How to identify this pattern on HRCT scan?



Answers :

(1) Mutiple discrete centrilobular nodules with linear branching pattern (arrow) are seen, representing tree-in-bud appearance. These imaging findngs are most commonly seen in pulmonary tuberculosis.

(2) Tree-in-bud appearance represents an endobronchial spread of infection, given the proximity of small pulmonary arteries and small airways.

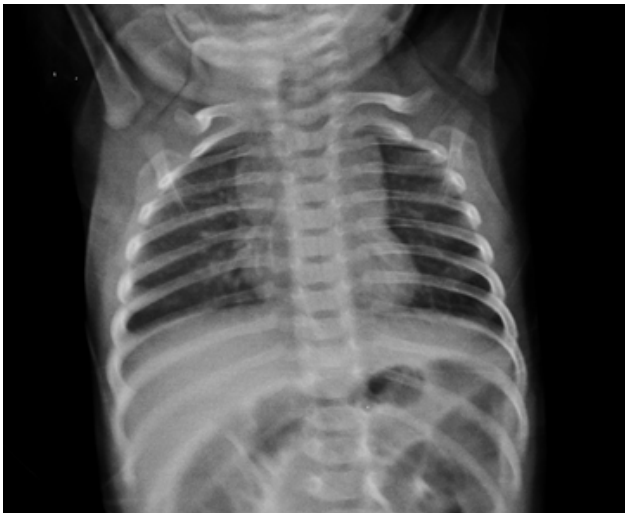
(3) Using maximum intensity projection (MIP) images facilitates detection of centrilobular nodules and their branching appearance.

Quiz 2

Radiograph of chest of a 20 day old neonate who presented with dyspnea and cyanosis.

Questions :

(1) What is the diagnosis?
(2) What is TAPVR?
(3) What forms the snowman appearance on chest radiograph?



Answers :

(1) There is widening of superior mediastinum, the configuration of heart and superior mediastinal borders resembling a snowman. This is seen in total anomalous pulmonary venous return (TAPVR) (Supracardiac type). It is also referred to as the "figure of 8 sign".

(2) Total anomalous pulmonary venous return (TAPVR) is a cyanotic congenital heart anomaly with abnormal drainage of entire pulmonary venous system. All systemic and pulmonary venous blood enters the right atrium and nothing drains into the left atrium. A right to left shunt is required for survival and is usually via a large patent foramen ovale or atrial septal defect.

(3) The dilated vertical vein on the left, brachiocephalic vein on top and the superior vena cava on the right form the head of the snowman, while the body of the snowman is formed by the enlarged right atrium.

Department of Radiology, Picture This by Jankharia, Mumbai, Maharashtra 400004
[1]MD, DNB (Radiology)
[2]MD, DMRD (Radiology)

Student's Corner

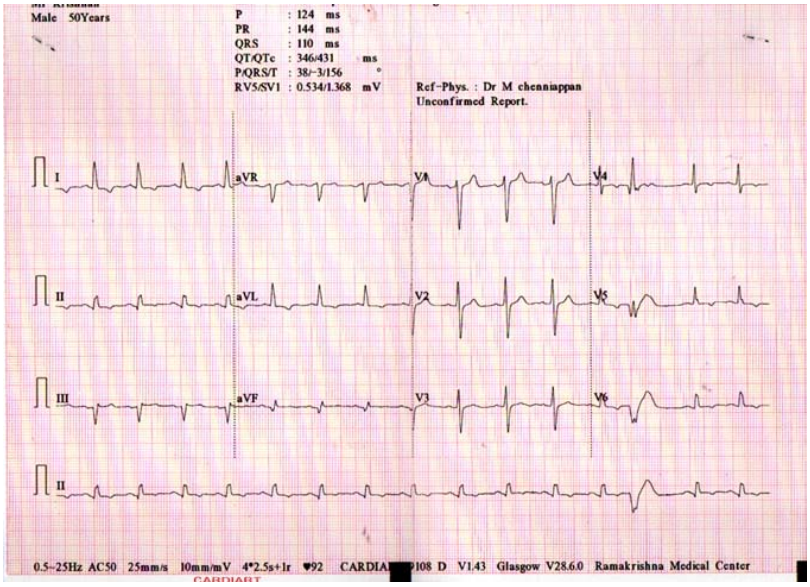
Become a Sherlock Holmes in ECG

M Chenniappan[1]

Series 8 :

"Premature Predictions"

Routine ECG of 50 years old patient with known CAD.



Questions :

(1) Describe all ECG changes
(2) Why is this clue?
(3) What are practical implications?

Answers :

ECG CHANGES :

ECG shows normal sinus rhythm with chronic stabilized phase of inferior wall myocardial infarction (IWMI). There are anterolateral and high lateral minor T wave inversions. The inferior wall infarction is likely to be due to right coronary occlusion because of the deepest Q is seen in LIII. In addition, there is a ventricular premature depolarization (VPD) in V4,V5, V6 and rhythm strip of LII. This VPD shows negative QRS complex in V6 suggestive of LV origin and negative QRS in LII is suggestive of inferior origin. So this VPD is likely to come from left posterior fascicular distribution area which is infarcted. In addition, VPDs in V4,V5 show pathological Q wave with small qR complex in V4, QRS complex in V5. This pattern is suggestive of chronic MI or scar in this region,although the basic sinus beats are not showing the infarct pattern. Infarction was diagnosed from the morphology of a VPD when it has a QR or QRS pattern with Q wave greater than or equal to 0.04 second. Morphologic analysis of VPDs had a low sensitivity but high specificity and high predictive value for the diagnosis of MI. In some ECGs, angiographic MI had no MI according to standard electrocardiographic criteria, but did have an MI manifested by VPB morphologic analysis. Despite low sensitivity, analysis of the morphology of VPBs may be useful for the diagnosis of MI when the morphology of sinus beats is not diagnostic. Therefore, VPD analysis is complementary to the standard electrocardiographic diagnosis of MI.

CLUE :

The ventricular premature beats are predicting following features

1. The site of origin; left posterior fascicular area
2. VPDs are arising from infarct area itself
3. VPDs are unmasking the chronic MI or scar in low septal and anterolateral areas even though the sinus beats are not showing the infarct pattern.

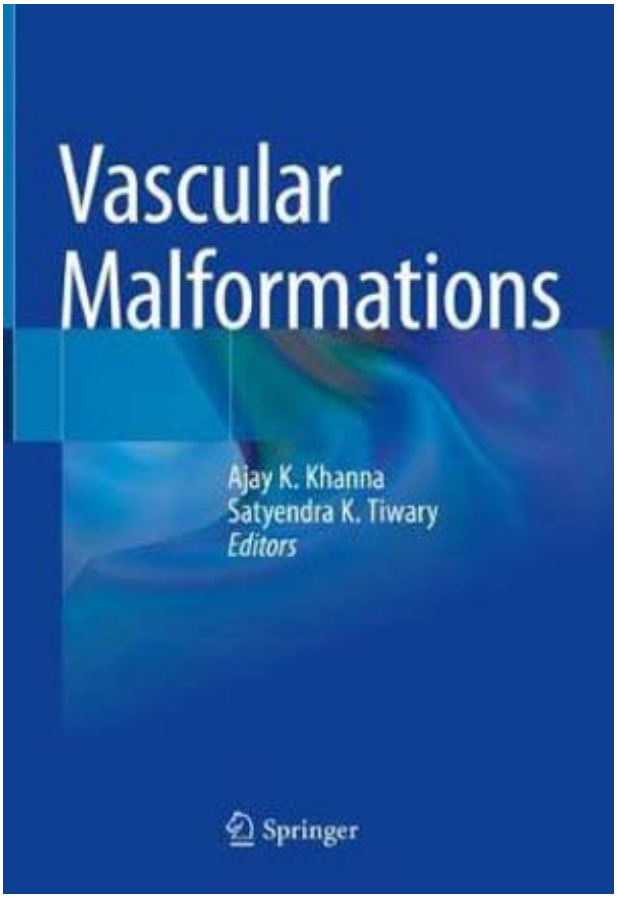
Because of these predictions by ventricular premature beats the clue of "Premature Predictions" is given.

PRACTICAL IMPLICATIONS :

In addition to IWMI , the VPD has unmasked additional MI in low septal and lateral areas which may need detailed investigations such as ECHO for LV function, Holter to decide about the malignancy of VPDs and coronary angiography to decide about revascularisation. The further management of CAD and this VPD depends upon the results of these investigations.

[1]Adjunct Professor, Dr MGR Medical University, Tamilnadu; Senior consultant cardiologist, Tamilnadu; Ramakrishna Medical Centre, Apollo Speciality Hospital, Trichy

Book Review



Vascular Malformations by Ajay K Khanna, Satyendra Kumar Tiwary (Eds), Vascular Malformations, Springer 2021:1-303. https://www.springer.com/gp/book/9789811597619, eBook : 117,69 •, Hardcover : 145,59 •

VASCULAR Malformations are fairly common disfiguring conditions which are a perplexing and challenging problem to manage.Though benign in nature, they are difficult to treat and in many cases, impossible to cure. It would require decades of experience and loads of wisdom before one can even think of writing on such an esoteric topic. Prof Ajay K Khanna, former Head of the Department of General Surgery at the Institute of Medical Sciences (IMS), Banaras Hindu University (BHU), Varanasi, India has written several books on vascular surgery such as Manual of Vascular Surgery (Jaypee), Ulcers of the Lower Extremity (Springer) and Varicose Veins Current Trends (Springer) and is an Internationally renowned expert on vascular diseases. He has now brought out a 300-page richly-illustrated monograph on vascular malformations in which a galaxy of authors from all over the country and even abroad (Bangladesh, Nepal, Poland, South Korea and USA) have covered history, epidemiology, approach, investigations and management, including medical, surgical, laser, endovascular and radiological, of various types of vascular malformations in general. In addition, each vascular malformation is individually addressed in one of the 22 chapters. Even genetics and quality of life issues have been covered.

The only deficiency I could find in the otherwise exhaustive book was no mention of filaria/ filarial/filariasis (probably because the chapter on lymphatic malformations is written by authors from Poland; an editorial note on the topic from the Editors should be appended in the next edition).

While it does suffer from the usual problems of non-uniformity of size (length of the chapter ranges from a mere 8 to as many 42 pages) and quality (Chapter 15 has 40 images while Chapter 14 has no images at all) of chapters of a multi-author book, Dr Khanna and his co-editor DrSatyendra K Tiwary, need to be complimented for having produced a virtual treatise on such an important, yet neglected, group of disorders. Vascular Malformations will become an authoritative reference book for managing patients and for reporting interesting cases with vascular malformations; it should find a place in the library of any Medical Institution all over the world.

Professor of HPB Surgery, Mahatma Gandhi Medical College & Hospital (MGMCH), Jaipur, Rajasthan, email - vkkapoor.india@gmail.com

V K Kapoor

Letters to the Editor

[The Editor is not responsible for the views expressed by the correspondents]

Management of Oral Contraceptives Induced Cerebral Venous Thrombosis, Hemorrhagic Infarction Presenting with Left Hemiparesis and Isolated Left Upper Limb Simple Focal Seizures

Sir — A 31 years old female, class-2 obesity (108kg) presented with sudden onset of shaking left upper limb intermittently which is associated with weakness and numbness since 2 hours. One episode of similar shaking of left upper limb 12 hours back, which was there continuesly for 3minutes, subsided by itself and not associated weakness and numbness. Patient is known case Polycystic Ovarian Disease(PCOD) and having irregular menstrual cycles since 5 years was on life style and Metformin. History of excessive menstrual bleeding since 3 months and diagnosed to have dysfunctional uterine bleeding with PCOD and she is on Tab Desogestrel (150mcg) and Ethinyl Estradiol (20mcg) orally once day since 15days as suggested by her Gynecologist. Metformin was stopped 15days back. Not known case of hypertension, diabetes mellitus.

On examination patient was anxious, conscious and well oriented. Heart Rate(HR) 108/minute, Non invasive Blood Pressure(NIBP)-136/92 mmHg. Saturation (SpO_2)-98%, Respiratory Rate(RR)-22/minute. Neurological examination revealed left upper limb and lower limb weakness present, able to left with difficulty but not against resistance (motor power 4/5). Sensory examination was normal. Witnessed left upper limb focal seizures while examining her in emergency room, she was conscious, responding while she was having seizures which continued next 3 minutes then subsided. Patient was given levetiracetam 1g Intravenous(IV) infusion, stabilized. Case discussed with neurophysician and MRI brain with MR venogram was done. Imaging suggestive of right parietal hemorrhagic infarction and paucity of the flow signals across the right parietal convexity; CVT. Patient was shifted to Intensive Care Unit(ICU) and started on Enoxaparin 60mg subcutaneous- twice day(BD), Levetiracetam-500mg IV(BD), Mannitol 20mg IV thrice day(TID), Citicoline 500mg IV(BD), Dexamethasone 4mg IV(TID). Neurosurgeon opinion was sought- no neurosurgical intervention and advised to medical line of management.

Hemoglobin 7.5gm%, Total count 9720/Cmm, Platelet count 4.9lakhs, Blood urea 26mg/dl, Creatinine-0.7mg/dl, Serum Sodium 136mmol/l, Potassium 3.6mmol/l, Chloride 105mmol/l. Random blood sugar-131mg/dl, Liver Function Tests and coagulation profile was normal, arterial blood analysis showed mild metabolic acidosis. Electrocardiogram was showing normal sinus rhythm.

ICU-DAY_2, Patient was conscious, oriented and haemodynamically stable. Upper limb and lower limb motor weakness present. Patient had one episode of similar focal seizures; patient was given Fosphenytoin 1.5g IV infusion. Inj Levetiracetam increased to 1g(BD) and continued with Fosphenytoin 150mg IV(BD). Electroencephalogram normal, Echocardiography normal, bilateral lower limb venous doppler normal. Serum Homocysteine levels 32.4mcmol/L. Vitamin B12 levels 18pmol/L. Patient was transfused with one unit of packed cells and patient was started on Homecheck capsule (Folic Acid,Methylcobalamin,Pyridoxine) and Acitrom 2mg(OD) orally. Inj Renerve 1mg IV(OD) added.

ICU-DAY-3, Patient complained of severe headache. Fundoscopy was suggestive bilateral symmetrical mild papilledema. Suspected intracranial hypertension, Mannitol 20mg increased to four times day(QID), started on oral Glycerol 30ml(TID) and Analgesics(Tab-Granil). Physiotherapy for left upper limb and lower limb started. Repeat hemoglobin-9.5gm%.

ICU-DAY-4, Patient was conscious, oriented. No more episodes of seizures, headache. Patient repeat INR was 2.5. Enoxaparin stopped, continued with tab Acitrom 2mg(OD), Fosphenytoin IV stopped added Tab Phenytoin 100mg(TID). Levetiracetam and Citicoline converted to oral medication and shifted to ward. Next day patient was discharged.

Discussion — Oral contraceptive has been widely known risk factor for Cerebral Venous Thrombosis.[1] Our patient was on oral contraceptives pills since 15days started for her dysfunctional bleeding and had paucity of flow in right parietal convexity suggestive of CVT. It was often seen in clinical reports that Venous Sinus Thrombosis leads acute infarcts or associated with hemorrhage after infarction.[2] Our patient had acute right parietal hemorrhagic infarction. It has been widely reported that Epilepsy is one of the common clinical manifestations of CVT[3,4].

Many articles and studies revealed CVT causing seizures but presence of isolated single limb focal seizures without altering higher mental functions and without postictal altered sensorium like in our case is rare and this focal seizures not responded to monotherapy, Levetiracetam and Phenytoin both were needed. Headache is the most common symptom and is present in 90% of cases; in 25% of patients, it is the only symptom reported[5]. This Headache Syndrome can range from a common Migraine to clear features of raised ICP,[6] where papilledema might also be visualized with Fundoscopy. Our patient had severe headache day 3 of admission, Fundoscopy showed mild symmetrical papilledema hence hiked on antiedema measures. Anticoagulation is a cornerstone of treatment, even in the presence of hemorrhage[4]. Our patient had hemorrhagic infarcts not actual intracranial hemorrhage hence started on anticoagulation early. Following the immediate management of CVT, long-term Vitamin K antagonists, such as Warfarin, with a target International Normalized Ratio (INR) of 2-3 should be used[4]. Our patient was started on oral Acitrom on day 2 of admission and repeat INR was 2.5 on day 4. Homocysteine levels increased in healthy women after they started using OCP[7], hyper-homocysteinemia and OCP use may interact in a synergistic manner in the pathogenesis of Venous thrombosis[8]. Hyper-homocysteinemia was an important correctable risk factor of CVST in patients from Northern India and majority of them had either low vitamin B12 level or *MTHFR* mutation[9]. Our patients homocysteine level was on higher side, Vitamin B_{12} level was low, we can assume OCP use and hyper-homocysteinemia, low

Vitamin B_{12} synergistically caused CVT.

Conclusion — OCP use, increased levels of homocysteine levels and lower vitamin B_{12} caused CVT with hemorrhagic infarction in our patient which associated isolated left upper limb focal seizures(rare clinical phenomena) and left hemiparesis responded well to anticoagulation and bi-anticonvulsant therapy.

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Pateel GNP[1]
Praveen Kumar S[2]
Manjunath B S[3]
Ramesh Somayayi[4]

Rajshekar Multi Speciality Hospital, Bengaluru, Karnataka 560078

[1]DNB (Anesthesiology), ICU Resident, Department of Critical Care and Corresponding Author

[2]DM (Neurology), Consultant Neurologist

[3]DNB (Anesthesiology), Senior Consultant Intensivist

[4]MD (Obstetrics and Gynaecology), Consultant Chief

Infectious waste from a COVID-19 Laboratory

Sir — On March 11, 2020, the WHO declared COVID-19 as a pandemic that changed the Global Health scenario. Person-to-person spread of SARS-CoV-2 occurs mainly via respiratory droplets. COVID-19 can also occur if a person touches a surface contaminated with SARS-CoV-2 and then the hands come into direct contact with mucous membranes such as the eyes, nose, or mouth. A meta-analysis described the incubation period of SARS-CoV-2 ranging from 2-17 days in human to human transmission. The survival period of SARS-CoV2 is important in formulating policies in proper health care waste management. The virus remains viable for 3 hours in aerosols, upto 72 hours in plastics and stainless steel or could survive on inanimate surfaces, ie, metal, glass, or plastic, for a period of 9 days. Therefore improper disposal of infectious waste from a laboratory can increase the spread of the virus in the community.

India has implemented comprehensive legislative Biomedical Waste (BMW) management guidelines in 2016 and amendments were added thereafter. Healthcare waste comprises the waste generated by healthcare facilities, medical laboratories and biomedical research facilities. As a provider of COVID-19 testing facilities, the laboratory deals with infectious healthcare waste like contaminated body fluids, PPE, gowns, masks, shower caps, shoe covers, goggles, face shields, etc. The other waste that has increased significantly are the waste generated from using test kits and General Healthcare waste which is non hazardous. All the laboratory waste were pre-treated and discarded in proper manner in order to prevent the spread of the virus.

There were dedicated waste collection areas in the sample labeling room, sample extraction room, PCR room, PCR donning area. Double layered bar coded yellow bags are used in the laboratory to ensure that there were no leaks. These bags are tied tightly with duct tape and sprayed with 1% sodium hypochlorite solution. The Biomedical wastes are finally stored temporarily in a designated room from where it is collected daily by authorized staff of the Common Biomedical Waste Treatment and Disposal Facility (CBMWTF). The designated room is sprayed daily with sodium hypochlorite solution. Therefore, adequate infrastructure and real time supervision will help in implementing proper waste management in a stringent manner.

Separate record is maintained for the waste generated by the COVID laboratory. Prior to COVID testing, the infectious waste generated in the department was negligible. During the last 15 months of COVID testing, there was a drastic increase in COVID wastes from approximately 100 to 1200kgs/month with an average 457kgs per month. During the first wave, the waste was high (1028kgs) during the months of August/September 2020 and in the second wave, it was high (1965kgs) in May and June 2021.

At present the department has performed approximately 2,15,000 tests. Therefore bigger laboratories which perform double the number of tests will be churning out a huge amount of infectious waste. Therefore, it is crucial to document the amount of waste generated in order for the Health authorities to take special measures to deal with the increased BMW. They can formulate appropriate policies for adequate infrastructure and human resources to handle the BMW.

Saramma Mini Jacob[1]
K Mary Sushi[2]
K Sivasangeetha[3]

The Tamil Nadu Dr MGR Medical University, Tamil Nadu 600032

[1]MD, Professor, Department of Experimental Medicine and Corresponding Author

[2]PhD, Research Officer, Department of Siddha

[3]MD, Associate Professor, Department of Experimental Medicine

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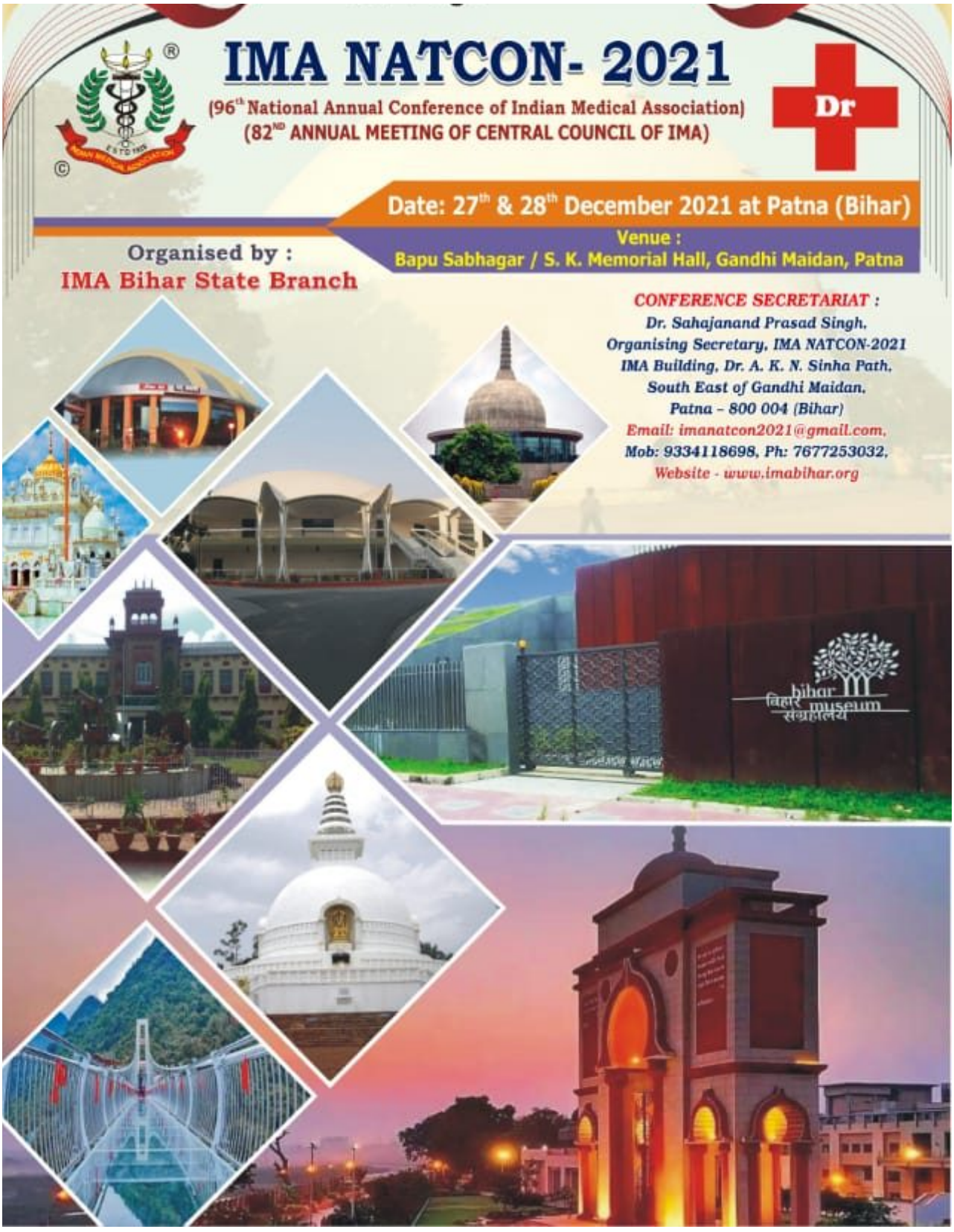
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Registration No. KOL RMS / 476 / 2020 - 2022

RNI Regd. No. 2557/1957
Vol. 65, No. 10, October 2021, Kolkata

Date of Publication : 20th October, 2021

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